MP60-16

Cell Cycle Progression score and PTEN as prognostic factors for metastasis in intermediate- and high-risk prostate cancer overall, and in those who also received salvage radiotherapy

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INTRODUCTION

The cell cycle progression (CCP) score and PTEN have never been evaluated together for metastasis-free survival (MFS) in a prostatectomy (RP) cohort of intermediate and high risk (IHR) prostate cancer (PCa), nor in IHR patients who also received salvage radiation (SRT) alone or with androgen deprivation (SRT+ADT). We evaluated CCP score, and PTEN in both contexts.

METHODS

Men received RP at Johns Hopkins from 2007-2015. Paraffin-embedded RP tissue was analyzed blind to outcome at Myriad Genetics for CCP score with qRT-PCR, and PTEN by immunohistochemistry. For overall evaluation of CCP and PTEN a case-cohort sample of IHR men was selected. Separately, a cohort of IHR men with biochemical recurrence who received SRT or SRT+ADT were also sampled to evaluate men at particularly high risk of metastasis. MFS was analyzed with the proportional hazards model (weighted for case-cohort design for overall analysis), adjusted for CAPRA-S. The cell-cycle risk (CCR) score, a locked algorithm combining CCP and CAPRA-S was also analyzed in both contexts. Data were analyzed independently by Johns Hopkins and Myriad Genetics.

DATA: IHR CASE-COHORT

There were 41 metastasis cases and a subcohort of 174 (including 6 cases). Both groups had median age 59, and 83% were white. As expected cases had significantly higher percentage of NCCN high risk (51% vs 17%), non-organ confined tumor (89% vs. 40%), and Gleason grade group 3-5 (94% vs 36%). Table 1 compares CAPRA-S, CCP, CCR, and PTEN between the groups, with cases having a higher risk profile.

DATA: IHR SALVAGE RT / RT+ADT COHORT

172 men received SRT (n=97) or SRT+ADT (75); 17 developed metastasis. Median age was similar in men with and without metastasis (59-60), and there were no significant differences in PSA, Gleason grade group, RP stage, margin status or CAPRA-S. Table 2 compares CAPRA-S, CCP, CCR, and PTEN by metastasis status; men with metastasis again exhibited higher biomarker risk profiles.

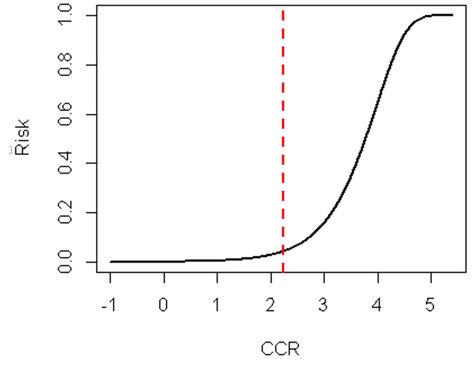
TABLE 1: IHR CASE-COHORT

Variable	Cases	Subcohort	p-value
CAPRA-S, median (IQR)	7 (5-9)	2 (1-6)	<.0001
CCP, median (IQR)	0.8 (0.4-1.7)	0.1 (-0.2-0.5)	<.0001
CCR, median (IQR)	3.4 (2.6-3.7)	0.9 (0.4-1.7)	<.0001
PTEN loss, n (%)	13 (42)	20 (12)	.0002

TABLE 2: SALVAGE RT/RT+ADT COHORT

Variable	Mets	Non-mets	p-value
CAPRA-S, median (IQR)	7 (4-9)	5 (4-7)	.056
CCP, median (IQR)	1.1 (0.6-1.6)	0.3 (-0.1-1.1)	.003
CCR, median (IQR)	3.3 (2.6-4.0)	2.2 (1.5-3.0)	.004
PTEN loss, n (%)	9 (53)	42 (27)	.031

METASTASIS RISK CURVE FOR CCR AT 5 YEARS



At CCR threshold = 2.242
5 year risk is 4.4%

TABLE 3: IHR CASE-COHORT MULTIVARIABLE MODELS*

Variable	HR (95% CI)	p-value	LRT**
MODEL 1:			
CCP, per unit	4.5 (1.7, 12.0)	.002	
CAPRA-S, per unit	2.0 (1.5, 2.7)	<.0001	0.010
MODEL 2:			
CCR, per unit	7.2 (3.9, 13.6)	<.0001	0.019
MODEL 3:			
CCR >2.242 vs. ≤2.242	30.5 (10.2, 91.3)	<.0001	0.043

* PTEN was not statistically significant in any model.
** LRT = p-value for likelihood ratio test vs. model with CAPRA-S

TABLE 4: SALVAGE RT/RT+ADT COHORT MULTIVARIABLE MODELS*

Variable	HR (95% CI)	p-value	AUC**
MODEL 1:			
CCP, per unit	1.9 (1.2, 2.9)	.007	
CAPRA-S, per unit	1.3 (1.05, 1.6)	.017	0.819
MODEL 2:			
CCR, per unit	2.3 (1.4, 3.6)	.0006	0.807
MODEL 3:			
CCR >2.242 vs. ≤2.242	3.2 (1.05, 9.9)	.041	0.707

* PTEN was not statistically significant in any model.
** AUC for CAPRA-S alone = 0.745

CONCLUSIONS

This is the first comparison, in a recent cohort of IHR men, of CCP and PTEN as risk factors for metastasis, and first evaluation in IHR men receiving SRT. In IHR men overall, and in IHR men who received SRT or SRT+ADT, CCP, but not PTEN, was significantly associated with MFS, adjusted for CAPRA-S. CCR, a fixed algorithm combining CCP and CAPRA-S was also significant in both contexts, and a previously defined CCR threshold of 2.242 was validated.

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