Favorable Intermediate-Risk Prostate Cancer Leads to Worse Survival Compared to Low-Risk Patients due to Adverse Pathology

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BACKGROUND

- Intermediate-risk (IR) prostate cancer is a heterogenous risk group.
- Potential "favorable" IR criteria have been proposed based on data from patients receiving radiation therapy, but their application to active surveillance remains uncertain.
- Preoperative clinical stage and Grade Group (GG) on needle biopsy are often upstaged or upgraded on surgical pathology. Evidence from the Johns Hopkins Radical Prostatectomy (RP) Database suggests no amount of risk stratification leads to comparable rates of adverse pathology for GG2 prostate cancer relative to low-risk (LR) patients.
- We aimed to quantify the rate of adverse surgical pathology for potential definitions of favorable IR prostate cancer compared to LR disease and assess implications for survival in the National Cancer Database (NCDB).

METHODS

COHORT

- Men undergoing RP with data on biopsy and surgical pathology from the NCDB (2009-2013) were included.
- Baseline and pathologic outcomes were compared for patients meeting clinically LR (GG1, ≤cT2a, PSA<10) or GG2 IR (GG2, ≤cT2b, PSA<20) disease.
- Adverse pathology was defined as ≥GG3, seminal vesicle invasion (pT3b), or lymph node metastasis (pN1)).

ANALYSIS

- Various definitions for favorable IR disease were explored including the Memorial Sloan Kettering definition (MSK; ≤GG2 with only one IR factor including GG2, cT2b, or PSA 10-20) and PSA and volume stratification of GG2 disease.
- Log-binomial regression compared rates of adverse pathologic findings while logistic regression assessed predictors of adverse pathology.
- Kaplan-Meier and adjusted survival curves based on Cox proportional hazards regression models compared overall survival (OS) between GG2 IR and LR groups as well as the impact of adverse pathology for GG2 IR patients.

CONCLUSIONS

- Adverse pathology is observed at a three-fold higher rate for patients with GG2 prostate cancer or those meeting the MSK definition for favorable IR disease compared to LR patients.
- The presence of adverse pathologic findings led to worse survival for men in the favorable IR risk group; favorable IR men as a whole experienced worse survival relative to LR men.

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RESULTS

DEMOGRAPHICS

- 51,688 LR and 42,720 GG2 IR men were included with GG2 IR men demonstrating slightly older age (61.2 vs. 59.5 years, p<0.01), higher baseline PSA (p<0.01), and greater number of positive cores with cancer (p<0.01).

ADVERSE PATHOLOGY

- GG2 IR vs. LR: RR 3.06 (2.95-3.17), p<0.001

Pathologic GG	Preoperative Risk Classification LR		GG2 IR	
N	51688	-	42720	-
≤2 (Gleason score ≤3+4=7)	48601	(94.0%)	35192	(82.4%)
3 (Gleason score 4+3=7)	2395	(4.6%)	5906	(13.8%)
4 (Gleason score 8)	483	(0.9%)	1041	(2.4%)
5 (Gleason score 9-10)	209	(0.4%)	581	(1.4%)
≥3 (Gleason score ≥4+3=7)	3087	(6.0%)	7528	(17.6%)
Seminal Vesicle Invasion	613	(1.2%)	2094	(4.9%)
Lymph Node Metastasis	85	(0.2%)	520	(1.2%)
Any Adverse Pathology	3519	(6.8%)	8888	(20.8%)

TABLE 1: Pathologic outcomes for men undergoing RP for LR and GG2 IR prostate cancer in the NCDB.

STRATIFICATION

- PSA and volume stratification slightly reduced the rate of adverse pathology for GG2 IR patients (PSA<10 → 19.2%, ≤2 Positive Cores → 16.0%)
- MSK Definition vs. LR: 19.9% vs. 6.8%; RR 2.92 (2.82-3.03), p<0.001
- Volume restriction significantly reduced the number of patients meeting criteria for the MSK favorable risk but only slightly improved the rate of adverse pathology (18.5% for those with <50% Positive Cores, 17.6% for those with ≤2 Positive Cores)

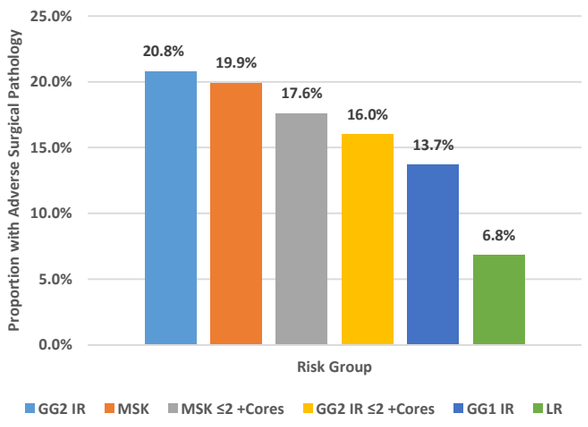

FIGURE 1: Rates of adverse pathology among potential definitions for "favorable" IR prostate cancer. Selected stratifications and examples are shown including the MSK definition.

PREDICTORS AND SURVIVAL OUTCOMES

- Age (OR 1.02 (1.02-1.03), p<0.001), higher PSA, and ≥3 Positive Cores were significant predictors of adverse pathology.
- GG2 IR patients had worse OS compared to LR patients in adjusted models (HR 1.24 (1.06-1.45), p=0.007) (Table 2).

TABLE 2: Cox regression models comparing OS for patients with GG2 IR and LR prostate cancer undergoing RP (also adjusted for race and median income quartile (not shown)).

		Univariable HR	95% CI High	95% CI Low	p-value	Multivariable HR	95% CI Low	95% CI High	p-value
Study Group	LR	REF	-	-	-	REF	-	-	-
	GG2 IR	1.51	1.31	1.74	<0.001	1.24	1.06	1.45	0.007
Age (per year)		1.06	1.05	1.07	<0.001	1.06	1.04	1.07	<0.001
PSA	<4	REF	-	-	-	REF	-	-	-
	4 to 10	1.41	1.17	1.72	<0.001	1.19	0.98	1.45	0.078
	10 to 20	2.18	1.57	3.02	<0.001	1.42	1.01	2.00	0.042
CCI	0	REF	-	-	-	REF	-	-	-
	1	1.98	1.67	2.34	<0.001	1.75	1.47	2.07	<0.001
	≥2	4.23	3.14	5.70	<0.001	3.29	2.43	4.45	<0.001
Number of Positive Cores	1	REF	-	-	-	REF	-	-	-
	2	1.29	1.03	1.62	0.029	1.20	0.96	1.52	0.116
	≥3	1.44	1.19	1.74	<0.001	1.25	1.03	1.53	0.023

- Adverse pathology was associated with worse OS for both the GG2 IR (HR 1.26 (1.03-1.54), p=0.023; Figure 2) and MSK definition (HR 1.30 (1.08-1.57), p=0.006) cohorts on multivariable Cox models.

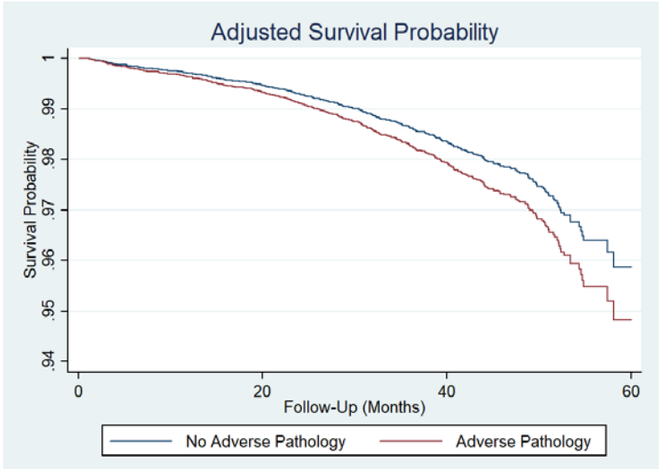

FIGURE 2: Adjust survival curves (based on Cox models) demonstrating the impact of adverse pathology on survival for GG2 IR patients (median follow-up: 31.1 months).