

Retrospective cohort review on the significance of pattern 3 positive margins in radical prostatectomy specimens

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Background

It is well understood that positive surgical margins following radical prostatectomy for prostatic cancer are associated with an increased risk of biochemical recurrence, compared with negative margins. A focus of research now has been to stratify the risk of BCR according to characteristics of the positive margin. The significance of the Gleason score of the cancer at the margin remains unclear and may have implications for both the prognosis and follow-up of these patients.

Aim

This study sought to determine whether Gleason 3 positive margins are more comparable in risk of biochemical recurrence (BCR) as compared to negative or higher-grade surgical margins.

Method

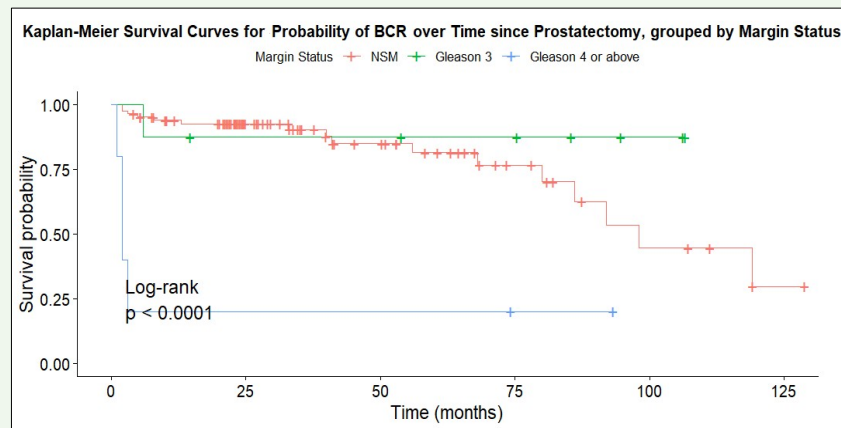
A retrospective cohort study was performed on men who had undergone robotic-assisted radical prostatectomy (RARP) for prostate cancer, performed by a single surgeon at Cabrini Health between 2015 and 2021. Following ethics approval, participant data was collected and grouped according to margin status and the Gleason score at the margin, if positive. Groups were compared in terms of the incidence of biochemical recurrence (BCR, defined as any recorded PSA >0.2ng/mL post-RARP), to assess whether there were significant differences between those with negative surgical margins (NSM), Gleason Pattern 3 at margin, and Gleason Pattern ≥4 at margin. The difference in incidence of BCR between these groups was assessed using the Fisher exact test. Kaplan-Meier survival analysis was performed to assess probability of BCR over time since prostatectomy, based on Gleason score at margin. A Cox proportional hazards model was applied to determine the association of Gleason score at margin and BCR risk, after adjustment for ISUP score of primary lesion and initial PSA level (known risk factors for BCR).

Conclusion

In our cohort of 103 patients, the difference in biochemical-recurrence free survival was not statistically significant in those with Gleason 3 at margin as compared to NSM, while those with Gleason ≥4 at margin had significantly higher risk. This finding has significant implications on prognostication, follow-up, and patient selection for salvage or adjuvant radiation post-prostatectomy, and prospective or randomised trials are warranted.

Results

Out of 118 total patients who underwent RARP, 103 met inclusion criteria for analysis. 85 patients had NSM, 8 patients had Gleason Pattern 3 disease at margin, and 10 patients had Gleason Pattern ≥4 at margin. Incidence of BCR was 18.8% (16/85) with NSM, 12.5% (1/8) in Gleason Pattern 3 at margin, and 80% in Gleason Pattern ≥4 at margin (8/10). Via Fisher's exact test, there was no statistically significant difference in incidence of BCR between those with NSM and Gleason Pattern 3 at margin ($p \sim 1$), however the increased incidence of BCR in those with Gleason Pattern ≥4 compared to NSM was statistically significant ($p < 0.0002$ with OR 17.25). Kaplan-Meier survival analysis was performed showing significant diversion of the survival curve for those with Gleason ≥4 at margin (log-rank test $p < 0.0001$), whereas those with Gleason 3 at margin and NSM demonstrated similar survival. Cox proportional-hazards regression analysis was used to adjust for confounding by known risk factors for BCR such as ISUP score of the primary lesion, and initial PSA. Post adjustment, the observed trend persisted with Gleason score of 3 at margin having no statistically significant difference in probability of BCR as compared to NSM ($p = 0.7$), whilst Gleason score ≥4 at margin carried significantly increased probability of BCR with HR 4.39 ($p = 0.003$).



Cox PH regression table for time to BCR by Gleason Score at margin, adjusted for variables for ISUP score of primary and initial PSA

Characteristic	HR [†]	95% CI [†]	p-value
Gleason Score at Margin			
NSM	—	—	—
3	0.70	0.09, 5.57	0.7
≥4	4.39	1.64, 11.7	0.003
ISUP score of Primary Lesion	2.04	1.38, 3.00	<0.001
iPSA	1.01	1.00, 1.02	0.11

[†]HR = Hazard Ratio, CI = Confidence Interval