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Pathological upgrading from Gleason 3+3 disease after radical prostatectomy: the implications for confirmatory testing

Deborah Kaye, Ji Qi, Ann Arbor, MI, Brian Lane, Grand Rapids, MI, Susan Linsell, Ann Arbor, MI, Richard Sarle, Dearborn, MI, James Montie, David Miller, for the Michigan Urological Surgery Improvement Collaborative, Ann Arbor, MI*

INTRODUCTION AND OBJECTIVES: The Michigan Urological Surgery Improvement Collaborative (MUSIC) is promoting the use of early confirmatory testing (i.e., MRI, genomics, or repeat biopsy) for better risk classification for patients considering active surveillance (AS). Because it is unclear whether such tests (which can be expensive, uncomfortable, and inconvenient) make sense for all men with Gleason 3+3 cancers at diagnosis, we examined the relationship between the number of positive cores at diagnosis and NCCN risk strata, and the frequency of pathological upgrading at the time of radical prostatectomy.

METHODS: We identified all men in the MUSIC registry initially diagnosed with Gleason 3+3 prostate cancer from 1/2012-8/2017 who had a prostatectomy within 1 year of diagnosis. We further classified these patients into NCCN very-low and low-risk disease. We then defined two categories of pathological upgrading: 1) the presence of any Gleason pattern 4 in the RP specimen; and 2) the presence of adverse pathology. Last, we compared the frequency of pathologic upgrading according to both the number of positive cores in the initial biopsy and NCCN risk category.

RESULTS: Among 1,866 patients with only Gleason 3+3 cancer on initial biopsy, 1,546 (83%) had very-low (278, 15%) or low-risk (1,268, 68%) disease. Pathological upgrading was both common and highly variable according to the number of positive cores on diagnostic biopsy ranging from 43% (1 positive core) to 79% (11 positive cores) for G3+4 ($p<.001$), and 24% (1 core) to 57% (12 cores) for adverse pathology ($p<.001$) (Figure 1). When evaluating by NCCN risk criteria, the rates of upgrading to >= G3+4 were 39% and 58% ($p<0.001$) and adverse pathology was present in 22% and 33% ($p<0.001$) for patients with very-low and low-risk cancers, respectively.

CONCLUSIONS: Adverse pathologic features at RP, including upgrading and upstaging, is common among patients initially diagnosed with G3+3 cancer. Although its frequency increases in synchronicity with both cancer volume and risk strata, the relatively high prevalence of upgrading even among men with a single core of G3+3 and those in the NCCN very-low risk group highlights the importance of early confirmatory testing to ensure optimal risk classification, and ultimately safe selection, of patients for AS.

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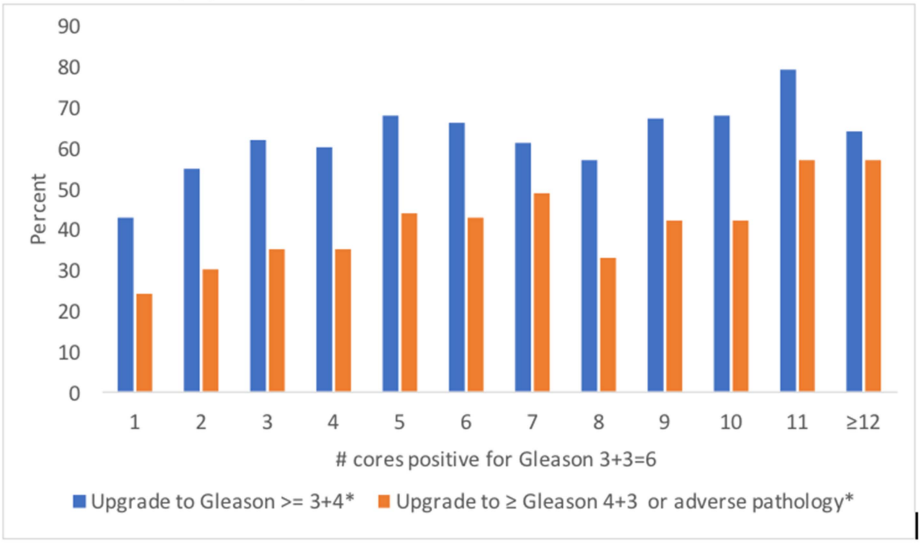
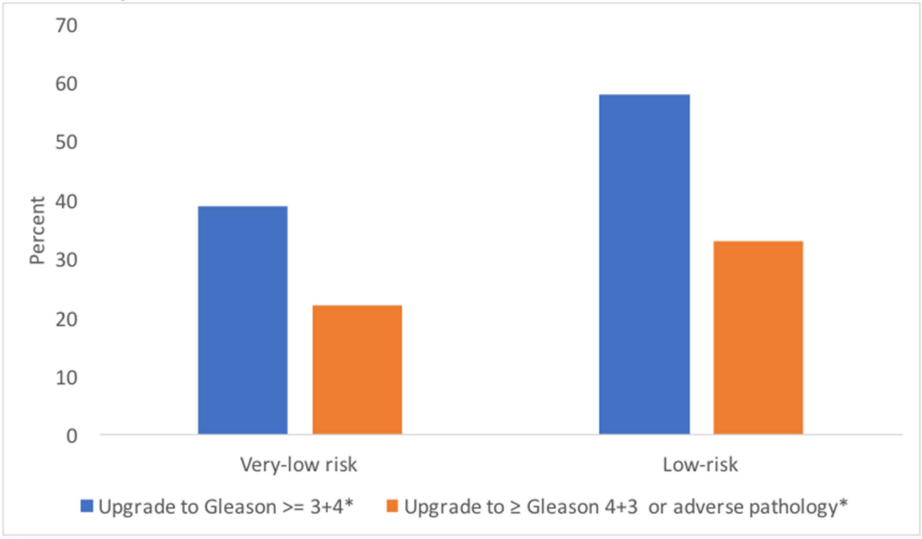
Figure 1. Percent of patients with pathologic upgrading or adverse features, by A) Number of biopsy cores positive with Gleason 6 and B) NCCN very-low and low-risk disease

A) Number of biopsy cores positive with Gleason 6



B) NCCN very-low and low-risk disease



* p <0.05

- Excluded patients with a ≥ 24 cores
- Adverse pathology is defined as predominant pattern 4 cancer and/or extraprostatic extension, seminal vesicle invasion, or lymph node involvement
- NCCN very-low risk disease is defined as: ≤T1c, ≤ Gleason 6, PSA < 10, < 3 cores positive for cancer with ≤50% cancer in each positive core; NCCN low-risk: ≤T2a, ≤Gleason 6, PSA<10