Are All D’Amico Intermediate Risk Prostate Cancer Patients Equal? Heterogeneity of Intermediate Risk Patients by Gleason Score
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Introduction and Objectives
The D’Amico risk stratification schema is a commonly used, validated predictor of prostate cancer outcomes. However, a significant heterogeneity of patients exists within the intermediate risk (IR) group. We analyzed intermediate-term oncologic outcomes of a large cohort of patients undergoing RALP and stratified the IR patients by Gleason score.

Methods
A database of 2008 consecutive RALP was stratified by standard D’Amico criteria. IR patients were then stratified by biopsy Gleason score (3+3=6, 3+4=7, 4+3=7). Pathologic outcomes and biochemical disease-free survival (BDFS) were compared among the standard and stratified groups. Biochemical recurrence (BCR) was defined as a single PSA >0.2 ng/ml.

Results
The cohort had a mean age of 69.6, mean PSA of 6.2 ng/mL, and median follow-up of 13.1 months. 950 patients were classified as D’Amico low-risk, 887 IR and 171 high-risk. Of the 887 IR patients, 144 had a biopsy Gleason 3+3=6, 553 were 3+4=7 and 187 were 4+3=7. Among the IR patients, as the biopsy Gleason score increased there was an increasing likelihood of extracapsular extension (14%, 29% and 42%, respectively, p<0.001), seminal vesicle invasion (2%, 6%, and 11%, p=0.005) and positive surgical margins (15%, 24%, 29% p=0.012). These differences translated to progressive worsening of intermediate-term biochemical outcomes (figure). Using Cox regression analysis, BDFS of the IR Gleason 3+3=6 group was not statistically different from the standard low-risk group (p=0.36) but was significantly better than IR 3+4=7 and IR 4+3=7 patients (p=0.03 and p=0.002, respectively). BDFS was also different between IR 3+4=7 and 4+3=7 patients (p=0.047). Preoperative PSA greater than 10ng/ml was also predictive of worse BDFS when controlling for biopsy Gleason score and clinical stage (p=0.001).

Conclusions
D’Amico IR patients demonstrate significant heterogeneity in both pathologic outcomes and BDFS. IR patients with a biopsy Gleason sum of 6 appear to have identical intermediate term BDFS as low-risk patients. Increasing biopsy Gleason scores from 3+3 results in higher likelihood of locally-advanced disease and BCR. IR patients with a biopsy Gleason score of 4+3 have significantly worse outcomes and may be suitable for clinical trials in the neoadjuvant setting.
Biochemical Disease Free Survival by D'Amico Risk Group with Substratification of Intermediate Risk Patients by Biopsy Gleason Score

D'Amico Risk Groups
- Low Risk
- Intermed. Risk Gleason 6
- Intermed. 3+4
- Intermed. 4+3
- High Risk

Cumulative Survival

Months