

Thotawaththage D., Fernando S.

**MORPHOLOGICAL HETEROGENEITY WITHIN GLEASON GROUPS: A PILOT
COMPOSITE AGGRESSIVENESS SCORE FOR MULTI-SITE PROSTATE CANCER
ASSESSMENT**

Tutors: PhD, associate professor Savosh V.V., assistant Vorobyova K.S.

*Department of Pathological Anatomy and Forensic Medicine with Advanced Training Course
and Retraining*

Belarusian State Medical University, Minsk

Relevance. Prostate cancer is the second most common malignancy in men worldwide. The Gleason grading system and its ISUP Grade Group refinement remain central to prognostication. However, these systems assign a single grade to inherently heterogeneous tumors, potentially obscuring clinically relevant inpatient morphological variation across biopsy sites.

Aim: to develop and pilot a Composite Aggressiveness Score (CAS) based on routinely observable hematoxylin and eosin (H&E) slide-level morphological features and to evaluate whether significant intra-patient, intra-Gleason-grade heterogeneity in this score exists across multi-site prostate biopsy specimens.

Materials and methods. A total of 50 prostate cancer histopathology slides obtained from five patients (10 slides per patient) were analyzed, supplemented by a review of current scientific literature. Each H&E stained slide was systematically evaluated for Gleason grade group (3-5). The presence or absence of cribriform architecture, intraductal carcinoma, stromal reaction, lymphovascular invasion, and gland crowding was recorded using a binary scoring system (1 = present, 0 = absent). Tumor extent and inflammation were assessed semi-quantitatively and categorized as mild (1), moderate (2), or severe (3). A Composite Aggressiveness Score (CAS) was calculated as the sum of these parameters. In addition, the predominant glandular morphology (round, angulated, or mixed) was documented without numerical scoring.

Results and their discussion. A total of 11 slides showed Gleason grade 3, 23 slides showed Gleason grade 4, and 16 slides showed mixed patterns (Gleason grades 3 and 4). In Gleason grade 3 specimens, the composite aggressiveness score (CAS) ranged from 4 to 7. In Gleason's grade 3+4 specimens, the CAS ranged from 4 to 9. In Gleason grade 4 specimens, the CAS ranged from 4 to 9 too. When a CAS of 4, 5, or 6 was considered, patients could belong to Gleason grade 3, 4, or 3+4, suggesting that tumor severity varies within the same Gleason group. All patients with cribriform morphology were classified as either medium severity (CAS 5-8) or high severity (CAS ≥ 8). No patient with cribriform morphology was classified as low severity (CAS ≤ 5). Furthermore, 14 out of 15 high severity cases exhibited intraductal carcinoma. Lymphovascular invasion (LVI) was uncommon, occurring in only 8 cases overall. However, when present, LVI was never observed in low-severity patients; all 8 cases occurred in either the medium or high severity categories.

Conclusions. These findings demonstrate marked inpatient heterogeneity within identical Gleason grade groups, suggesting that reliance on grade groups alone may underestimate underlying morphological diversity and tumor complexity. The proposed Composite Aggressiveness Score (CAS) offers a practical, morphology-based approach to capturing tumor complexity and may enhance risk stratification.