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Reimagining dry eye disease management-a multimodal approach targeting the key pathophysiological drivers

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Abstract

Purpose: Traditional dry eye disease (DED) diagnosis and subclassification often relies on limited metrics, failing to capture its complex heterogeneity. Aligning with the TFOS DEWS III framework, this study aimed to implement a novel, multimodal DED evaluation strategy, determining the prevalence of the pathophysiological DED drivers and identifying clinically relevant phenotypic clusters within a DED population. **Methods:** A prospective, cross-sectional study was conducted at a university-based clinic. A total of 615 participants (aged 20-45) meeting TFOS DEWS II diagnostic criteria underwent a comprehensive, standardized battery of ocular surface tests. These tests assessed nine predefined drivers across three domains: tear film (lipid, aqueous, mucin/glycocalyx deficiency), eyelid anomalies (lid closure, lid margin health), and ocular surface abnormalities (anatomical misalignment, cellular damage/disruption, primary inflammation/oxidative stress and neurosensory dysfunction). Cluster analysis was performed to identify distinct DED phenotypes based on these drivers. **Results:** The prevalence of the drivers varied considerably. Mucin/glycocalyx deficiency (identified by conjunctival staining) was most common (88%), while incomplete lid closure was least prevalent (24%). Other notable prevalences included aqueous deficiency (61%), meibomian gland dysfunction (43%), bulbar hyperaemia (48%), and reduced corneal sensitivity (37%). Cluster analysis revealed a robust four-cluster model (Silhouette score = 0.40), effectively partitioning the cohort into distinct subgroups. The clusters identified demonstrated a progressive increase in driver involvement and severity, with Cluster 1 associated with early signs (e.g., lid wiper and conjunctival staining) and Cluster 4 representing severe, multi-driver disease. **Conclusion:** This study confirms the heterogeneous prevalence of DED drivers in a clinical population. The identification of four distinct phenotypic clusters validates a shift from a binary spectrum DED classification towards a precision medicine approach. By deconstructing DED into its constituent pathological elements, this multimodal framework enables clinicians to phenotype patients and tailor targeted therapies to their dominant drivers, ultimately advancing personalized DED management.

Keywords

Author Keywords: Dry eye disease (DED); Diagnosis; Subclassification; tear film; eyelid; ocular surface; drivers
Keywords Plus: MEIBOMIAN GLAND DYSFUNCTION; LID-WIPER EPITHELIOPATHY; OCULAR SURFACE DISEASE; CORNEAL

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