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Pathobiology. 2025 Jul 26;1-14. doi: 10.1159/000547335. Online ahead of print.

Predictive Histopathological Markers for Upstaging to Invasive Carcinoma after a Biopsy Diagnosis of Ductal Carcinoma in situ of the Breast: A Hypothesis-Generating Systematic Review

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PMID: 40716433 DOI: [10.1159/000547335](#)

Abstract

Introduction: Around 25% of patients with a biopsy diagnosis of pure ductal carcinoma in situ (DCIS) will be upstaged to invasive breast carcinoma (IBC) after surgery. Because of this upstaging risk, patients with high grade DCIS frequently undergo a sentinel lymph node procedure (SLNP), which can cause surgery-induced morbidity. Presentation with a palpable mass increases the upstaging risk, but histopathological predictors are currently unclear. This PROSPERO-registered systematic review aims to identify which biopsy-based histopathological markers can predict the presence of IBC in the subsequent resection. These results might help to reserve SLNPs for selected high-risk patients, aiming to personalize treatment.

Methods: PubMed, Embase, and Scopus were searched for content using predefined search queries. Three reviewers independently screened the literature in Rayyan by applying predefined criteria and retained 36 reports. Studies including DCIS with micro-invasion were excluded.

Results: This systematic review comprised 18,475 patients. The median cohort size was 267 patients (range: 67-3,780). Most studies were retrospective (33/36). The median upstaging risk was 26% (range: 8-52%). The reports studied twenty-three histopathological and immunohistochemical features. Only seven features were investigated in multiple studies, all yielding contradictory results. For instance, thirty-three studies investigated nuclear grade, but only 18 reports demonstrated a significant association with upstaging, independent from cohort size.

Conclusion: No robust histopathological features can be recommended at present to reliably predict the upstaging risk to IBC after a biopsy diagnosis of pure DCIS. We discuss several hypotheses, aiming to explain these contradictory data. Ideally, large-scale multicentre prospective studies should be organized to answer this unmet clinical need.

Keywords: Ductal carcinoma in situ biopsy; Histopathological features; Predictive markers; Sentinel lymph node; Upstaging.

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