# Postoperative Radiotherapy Delay and Survival in Oropharyngeal, Hypopharyngeal, and Laryngeal Cancer: A Propensity Score-Matched, Site-Specific Analysis

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## Introduction

- The Commission on Cancer (2021) stipulates postoperative radiotherapy (PORT) within 42 days as the only HNC-specific quality measure.[1]
- Although PORT delays are linked to worse outcomes, its impact may differ by tumor site due to biologic and prognostic differences.[2]
- This study aims to evaluate the prevalence and survival impact of PORT delays in oropharyngeal (OPSCC), hypopharyngeal (HPSCC), and laryngeal (LSCC) squamous cell carcinoma (LSCC) using the national cancer database (NCDB).

## Methods

Included: histology of SCC, diagnosed ≥ 2015, adjuvant radiotherapy received

- OPSCC (n=15,845)
- HPSCC (n=895)
- LSCC (n=6,898)

*Excluded: non-primary tumors, metastatic disease, non-standard/palliative RT, receipt of neoadjuvant therapy, and cases with excessive treatment delays (>180 days)*

Meeting both inclusion and exclusion criteria

- OPSCC (n=11,126)
- HPSCC (n=481)
- LSCC (n=4,690)

Propensity-score matched: arm 1=timely; arm 2=delayed PORT

- HPV+ OPSCC (n=1,901/arm)
- HPSCC (n=87/arm)
- LSCC (n=1,134/arm)

- **Outcomes**: Primary = overall survival (OS); also assessed 2- and 5-year OS.
- **Analyses**: Kaplan-Meier, Cox regression, and predictors of PORT delay assessed by Poisson regression.
- **Bias Control**: Propensity score matching (1:1 nearest-neighbor) adjusted for age, sex, race, comorbidity, education, income, insurance, facility type, clinical stage, year of diagnosis, tumor size, and tumor location before OS comparison.
- **HPV Status**: OPSCC HPV status imputed using validated surrogate model.

## Results

- **Prevalence of delayed PORT:** Highest in HPSCC (66%), then LSCC (54%), followed by OPSCC (51%).
- **Survival outcomes:** No significant OS difference between timely and delayed PORT in HPV+ OPSCC or HPSCC, but delayed PORT associated with worse OS (HR: 1.27, 95% CI: 1.07-1.50).

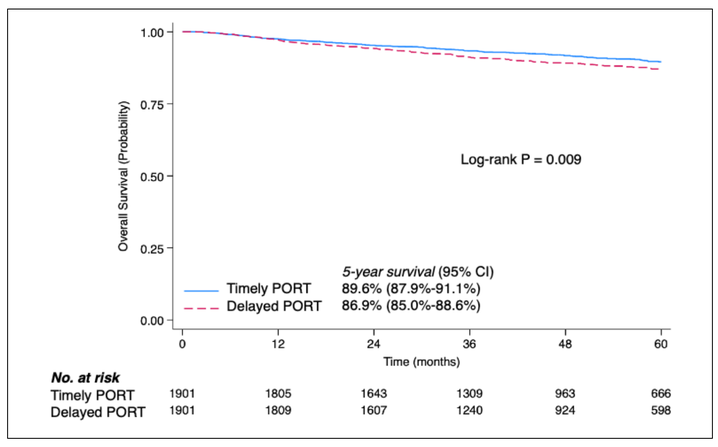


**Figure 1: OPSCC (HPV+)**

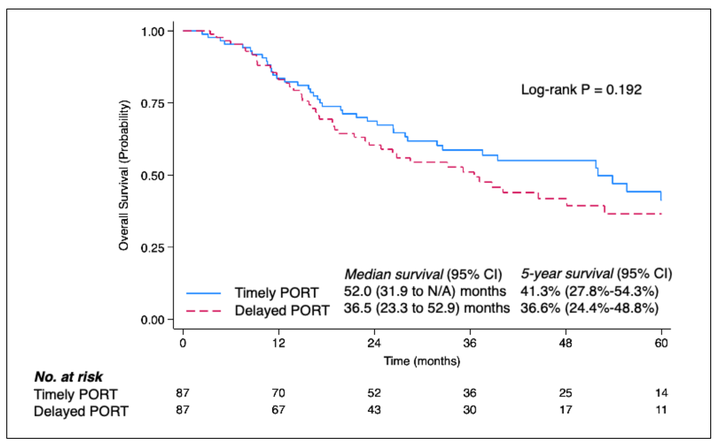


**Figure 2: HPSCC**

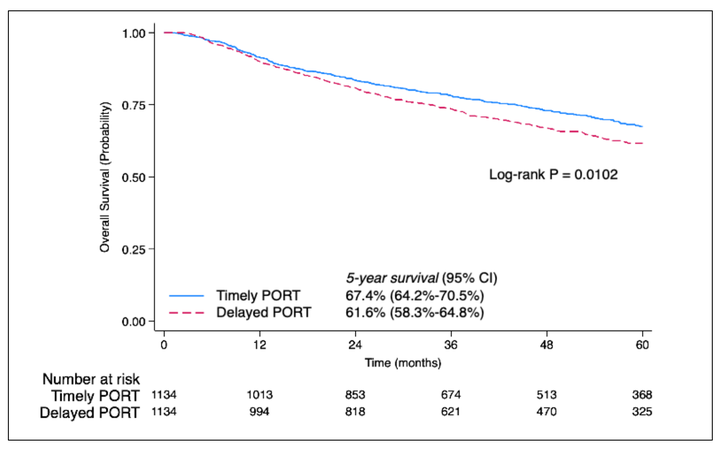


**Figure 3: LSCC**

- **Predictors of delayed PORT:**
  - Across all three sites:
    - Advanced T stage consistently predicted PORT delay, highlighting the impact of more complex disease on timely adjuvant therapy.
    - Surgical approach also played a role, with minimally invasive techniques (endo-/laparoscopic or robotic) linked to delayed in cohorts.
  - Beyond these shared patterns, distinct site-specific predictors of PORT delay emerged:
    - OPSCC (HPV+): Delays clustered in the years 2019 and 2021 (COVID-19 era) and in patients with nodal upstaging.
    - LSCC: Tumor differentiation (moderately/poorly differentiated) nodal involvement (pN1, pN3), postoperative readmission, and pandemic years.
- **Strengths**: Large representative NCDB cohort enabled robust, site-specific analysis of PORT delay, including in understudied sites like HPSCC. Use of propensity-score matching reduced bias from patient- and system-level factors.
- **Limitations**: NCDB lacks granular clinical and treatment details and reliance on overall survival may be confounded by non-cancer mortality.

## Conclusion

- PORT timing is a measurable, actionable quality metric, and institutional interventions such as care coordination and navigation have successfully reduced delays.[3]
- Future directions: **refinement of the 42-day benchmark with disease-specific cutoffs**, or allowances for clinical variability, in order to improve its relevance as a quality metric across HNC subsites.

## References

1. Cramer, J. D. *et al.* National evaluation of multidisciplinary quality metrics for head and neck cancer. *Cancer* **123**, 4372–4381 (2017).
2. Graboyes, E. M. *et al.* Effect of Time to Initiation of Postoperative Radiation Therapy on Survival in Surgically-Managed Head and Neck Cancer. *Cancer* **123**, 4841–4850 (2017).
3. Duckett, K. A. *et al.* Delays Starting Postoperative Radiotherapy Among Head and Neck Cancer Patients: A Systematic Review and Meta-Analysis. *Otolaryngol Head Neck Surg* **170**, 320–334 (2024).

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