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# Survival and selected outcomes of older adults with locally advanced head/neck cancer treated with chemoradiation therapy

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ABSTRACT

*Objectives:* Chemoradiation therapy (CRT) remains a potentially curative treatment in patients with locally advanced head/neck cancer (LA-HNC). However, survival and other outcomes in older patients with head/neck cancer receiving chemoradiotherapy are not well established. This study was performed to elucidate selected outcomes in this patient population.

*Materials and Methods:* Retrospective study of LA-HNC patients ≥70 years of age who had received 5-fluorouracil-hydoxyurea-based CRT with a minimum of 3 years of follow up after therapy initiation was performed. Pre-treatment patient- and cancer-related characteristics were recorded. Survival data in addition to gastrostomy tube utilization, swallowing function, and hematologic toxicity were captured.

*Results:* Eighty-nine patients treated between 1997 and 2009 were eligible for analysis (median age, 76 years; range, 70–94; male, 61%; ECOG PS, 0–1 43%; stage IVA/B, 71%). 86 were evaluable for survival analysis. 5-year overall and event-free survival were both at 32% with a median follow-up time of 39.2 months. The majority (86.5%) were able to complete all planned treatment cycles. A significant proportion of patients, however, required gastrostomy tube during CRT (62%) and developed aspiration during swallowing evaluation post-treatment (44%). Several patients required hospice (9%) or skilled nursing facility (13%) referrals during treatment.

*Conclusion:* Select older adults with LA-HNC can still experience long-term benefits despite 5-year survival rates lower than those historically reported in younger patients undergoing identical CRT regimens although potentially at higher risk for acute toxicities. Assessment and selection of those who can tolerate more intense combined-modality strategies and their long-term outcomes merit further larger, prospective studies.



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## 1. Introduction

Despite the rise of human papillomavirus-related oropharyngeal cancers among relatively younger adults, head and neck cancers remain a common cancer among older adults, with a median age of diagnosis in the early 60s, with over half of affected patients diagnosed with locally advanced disease (i.e., stages III–IVB).[1] As a result, concurrent chemoradiotherapy (CRT) remains a potentially curative treatment approach for the majority of these patients. The use of CRT has led to improved organ preservation, locoregional control rates of up to 95%, and 3 to 5 year progression-free survival (PFS) and overall survival (OS) rates approaching 60–80% and 60–70%, respectively.[2–8]

However, the role of CRT in older adults with locally advanced head/neck cancer (LA-HNC) remains under-explored for several reasons. There is evidence that CRT confers an absolute survival benefit based on a recent meta-analysis of clinical trial data.[8,9] However, older adults are under-represented in cancer clinical trials in general[10] and several of the seminal CRT studies either excluded older adults or had patients with a median age ≤60 years, often incorporating cisplatin-based chemotherapy that might be more difficult to administer safely to older adults.[2–4,6] Single institution-based studies have demonstrated that older adults with LA-HNC may still derive similar benefits of locoregional control and survival with CRT.[11–13] These potential benefits, however, are tempered by higher risks for toxicity. Chemotherapy for relapse and metastatic disease in older adults with head/neck cancer can achieve similar response rates and time to progression benefits, yet with higher attendant risks such as increased rates of renal, gastrointestinal and hematologic toxicities.[14] Similar findings have also been demonstrated with radiotherapy including observations that advanced age is a risk factor for late radiotherapy related toxicities such as swallowing dysfunction, fistula formation and gastrostomy tube dependence.[15–17]

These knowledge gaps in assessing the role of CRT in older adults with LA-HNC have led us to examine our own institutional experience in those aged 70 years and older who have undergone CRT. The aim of this study was to qualitatively examine the following key clinical outcomes in this patient cohort: event-free and overall survival; hematologic and non-hematologic treatment-related toxicities; unplanned hospitalizations and their reasons for admission; and rates of gastrostomy tube placement and retention.

## 2. Patients and Methods

This is a retrospective medical record review of patients with newly diagnosed, head/neck squamous cell carcinomas (excluding nasopharynx and salivary gland tumors) with stages II–IVB disease treated with definitive concurrent CRT at the University of Chicago Medical Center from January 1, 1997 to October 1, 2009. Patients were identified through our internal head/neck cancer database in radiation oncology, which included patients both on and off study protocols. The date of the last review for this study was September 1, 2012. Institutional review board approval was obtained prior to initiation of the study. Patients with stage II cancers deemed "high-risk" (e.g., unresectable tumor with estimated 2-year life expectancy ≤10% with RT alone) recommended to receive definitive CRT by the treatment team through tumor board consensus were also included based on the institution's experience in this group.[18–20] Limited surgical resection prior to CRT was allowed if it had been part of diagnostic and/or staging purposes. Treatment strategies incorporating induction chemotherapy and/or alternative radiation dosing (hyperfractionated and/or accelerated) were permitted for study inclusion. All patients were required to have been at least 70 years of age at the start of CRT. The majority of patients received 5-fluorouracil-hydroxyurea (FHX)-based CRT regimens during scheduled hospitalizations, whether on- or off-study, as part of the institution's preference for FHX-based regimens, which allows for avoidance of cisplatin-based toxicity and relatively more intensive radiotherapy strategies. Details of these combination regimens, including dosages and frequencies, have been described in prior studies.[18,19,21–25]

All patients were deemed generally fit to undergo CRT by a multidisciplinary team. All pre-treatment (i.e., baseline) evaluations included a history and physical examination; baseline laboratory testing including complete blood count and serum chemistries; swallowing evaluation incorporating a videofluoroscopic swallowing (VFS) examination; and CT imaging of the neck and chest. Comorbidity at baseline was captured utilizing the Charlson comorbidity index, excluding cancer diagnosis.[26] This score is summated with each comorbid condition assigned a different numerical value, with higher total scores associated with higher one-year mortality. Gastrostomy tube for nutritional support was recommended and placed when severe mucositis and/or dysphagia led to significantly decreased oral intake resulting in signs of severe dehydration, severe protein/calorie malnutrition, and/or weight loss ≥10% of baseline. Because of insufficient data and lack of routine evaluation in the records, other clinical factors such as tobacco use, alcohol use, human papillomavirus (HPV) status of the tumor, level of social support, and prior radiation exposure were not included a priori for analysis.

Event-free survival, overall survival and cause of death were assessed and recorded for up to 5 years post-CRT completion. Treatment response data were incomplete for many patients, so this was not included in the analysis (data not shown). Cumulative incidence of gastrostomy tubes was examined. In addition, the time from day 1 of CRT to gastrostomy tube placement (days) (i.e., gastrostomy tube placement latency) as well as time of tube placement to time of tube removal (days) (i.e., gastrostomy tube retention) was examined. Rates of gastrostomy tube revision and/or replacement were also recorded. Rates of aspiration were also evaluated with serial VFS examinations prior to, within one month of completion of, and at 6 and at 12 months following CRT if recorded.

Frequency, severity, and types of hematology/non-hematologic toxicities utilizing the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE), version 4.0, were evaluated.[27] Unplanned hospitalizations (i.e., hospitalizations during the off-week given the q2 week CRT schedule) during the course of CRT were examined and