390 INVITED

Lack of Benefit of Intensified Treatment Strategies in Elderly Patients With Squamous Cell Head and Neck Cancer

Abstract not received

391 INVITED

The Importance of Geriatric Assessment Using the "Frailty Index" Among Patients With Head and Neck Cancer Treated With Radiotherapy: Toxicity and Quality of Life

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Introduction: Elderly cancer patients more often suffer from comorbidity, diminished organ functions with impairment of daily vital functions and cognitive function. Biologic age as such is a poor marker for health risks. Frailty is commonly defined as a state of decreased resilience or vulnerability to stressors. Instruments for comprehensive geriatric assessment, such as the Groningen Frailty Index (GFI) provide information on the functional status of elderly cancer patients, including information on comorbidity, functional status, nutritional status and psychosocial status. The GFI has been developed as a simple screening instrument for frailty and a case finder for elderly patients who would benefit from integrated geriatric care. The GFI score ranges from 0 to 15. The purpose of this study was to determine the influence of the GFI score on acute and late toxicity and quality of life (QOL) among patients curatively treated with radiotherapy of chemoradiation for head and neck cancer.
Material and Methods: The GFI was used among patients with head and neck cancer treated with curative radiotherapy or chemoradiation at the department of Radiation Oncology of the University Medical Center Groningen. All patients were subjected to a standard follow up program, including prospective evaluation of acute and late toxicity, as well as health-related quality (EORTC QLQ-C30 and EORTC QLQ-H&N35). Frailty was defined in case of a GFI > 6. Acute toxicity was measured weekly during radiation and 6 weeks after completion of treatment according to the CTCAE v3.0. Late toxicity was measured every 6 months after radiation. QOL was assessed at similar time points.
Results: The study population was composed of 275 patients, of which 166 (60%) were male. The median GFI was 6. Thirty-nine percent (109 patients) were classified as frail.
At baseline, frail patients experienced significantly more head and neck cancer symptoms and toxicity and performed worse with regard to all functional dimensions of QOL and global quality of life.
Frail patients experienced significantly more acute toxicity, in particular acute xerostomia and sticky saliva, and swallowing dysfunction. After completion, frail patients recovered more slowly. After 12 months late toxicity was similar in both groups. Similar results were found with regard to patient-rated head and neck cancer symptoms and general symptoms. Frail patients scored worse on the general dimensions at baseline and at all time points after completion of treatment.
After correction for baseline scores, these differences partly disappeared.
Conclusions: The GFI is a significant prognostic factor for acute and late toxicity of curative radiotherapy of chemoradiation in head and neck cancer and for worse QOL. As a consequence, frail patients could benefit from more intense and integrated geriatric supportive care during and after treatment.

Scientific Symposium (Tue, 27 Sep, 09:00–11:00)
Managing the Side Effects

392 INVITED

Early and Late Side Effects Related to Surgery

Abstract not received

393 INVITED

Combination of Radiotherapy and Targeted Agents – What Should We Expect?

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The paradigm of combined radiotherapy and Cetuximab in head and neck cancer is assumed to represent the beginning of successfully combining radiotherapy with biologically targeted agents. Based on *in vitro* and *in vivo* studies many agents combined with radiotherapy have the potential to improve tumour control although pre-clinical data demonstrating clear improvement in therapeutic ratio is limited.
Combination of radiotherapy and systemic agents carries the risk of enhancing radiation induced toxicity and this is of particular relevance when treating to doses close to normal tissue tolerance. The increase in both acute and late effects of combined radiation with conventional systemic chemotherapy provides a model for recording the late effects of combination of radiotherapy with targeted agents. Some side effects of combined chemo-radiotherapy were recognised early and others, particularly if unexpected, with delay. The introduction of targeted biological agents with radiation requires phase I studies although the design aimed at assessing agents alone is not generally suitable for side effects of combined treatment which may occur months or years later. The presentation will review the available clinical data on the potential risks of combined radiotherapy and targeted agents and will suggest modern radiotherapy solutions to try and minimise some of these.

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Is It Time to Review the Common Toxicity Criteria in the Era of New Targeted Drugs?

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Targeted therapies exploit molecular features known to be upregulated specifically in neoplastic cells. Hence, it was hoped that by focusing on molecular and cellular changes that act by downregulating or "switching off" processes that are critical to cancer development or progression, targeted therapies may be less harmful to normal cells. Even though most of the targeted therapies produce less toxicity than standard cytotoxic agents, these expectations not always have been met.
The severity of adverse events related to the use of systemic cancer therapies is currently assessed using standard National Cancer Institute Common Toxicity Criteria (CTC). This system was developed primarily as a surveillance tool, at the time when most anticancer agents were administered intermittently, predominantly intravenously, and their toxic effects were transient. Thus, it was mainly designed to identify acute toxicity of a given agent, considering severity and level of necessary intervention. In turn, targeted therapies are typically administered daily, mostly orally and for prolonged periods of time. Although these drugs rarely cause severe toxic effects, subacute toxicity experienced continuously for several months may substantially affect patients' quality of life and activities of daily living. In consequence, this may incur poor compliance, dose reductions or treatment discontinuation. For example, whereas grade 1 or 2 nausea, diarrhea, muscle cramps or fatigue may be acceptable for a couple of days, they may turn out unbearable if become permanent. Similarly, rash severity relying heavily on body surface area coverage fails to account for the location of EGFR-associated rash confined typically to the face an upper trunk. Additionally, with the current recording system, adverse events that persist unabated for several months may remain underreported, and the maximally tolerated doses may be established improperly. Thus, objective assessment of long-term cumulative effects seems to be essential.
There is clearly a need for some modifications of CTC in the era of new targeted drugs. Reporting of adverse events not only should include their grade and attribution, but should also take into account their duration, the impact on patients' quality of life (bother items) and their physical functioning. Proper grading of adverse events should allow their proper management and dose modifications, but may also assist in investigating the relationships between some toxicities and treatment efficacy (for example skin toxicity accompanying anti-EGFR therapies). Although some modifications considering specificity of targeted therapies have already been introduced in the last version of CTC, further amendments are warranted.

395 INVITED

How to Follow up the Acute and the Late Toxicity With New Emerging Therapies?

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Cancer is a leading cause of death worldwide and accounted for 7.6 million deaths (around 13% of all deaths) in 2008 and the cancer deaths are projected to continue to rise to over 11 million in 2030. Cancer therapies typically include local regional (surgery and/or radiotherapy) and systemic, and a combination of local regional and systemic approaches. During past decades, many new therapies have been developed and all cancer therapies developed to date is associated with a spectrum of acute and late normal tissue toxicities and signs and symptoms of varying incidence and severity associated with these toxicities. However, there still issues in methods for reliable diagnosis, follow-up, report, and quantification of acute and late normal tissue toxicities.
Using lung cancer therapies as an example, a review of many of the issues involved in diagnosing, follow-up, reporting acute and late toxicities