The effect of NQO1 polymorphisms on prognosis of non-small cell lung cancer after postoperative radiation therapy

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Purpose: NQO1 is an enzyme that catalyzes the two-electron reduction of the more toxic quinone to less toxic hydroquinone. It is known that NQO1 may decrease the risk of cancer development in normal human tissue, and NQO1 polymorphism affect on the treatment outcome after chemotherapy in lung cancer. We investigated the effect of NQO1 polymorphism on radiation therapy through the difference of survival outcome by NQO1 different genotypes in non-small cell lung cancer (NSCLC) patients treated with surgery followed by postoperative radiation therapy.

Methods: One hundred and fifty-two patients (Male: 116, Female: 36) who were histologically proven NSCLC and treated with surgery and postoperative radiation therapy from Jan 2000 to Aug 2005 were analyzed. We determined NQO1 genotypes from peripheral blood of patients. NQO1 genotypes were classified as three groups, and each genotype had different enzymatic activities: C/C is the wild type with normal activity, C/T is the heterozygous type with decreased activity, and T/T is the homozygous mutation with no enzymatic activity. Thereafter, we analyzed the correlation between NQO1 genotypes and the survival outcome after surgery and postoperative radiation therapy. For the authenticity of genotype from peripheral blood, genotypic analysis was directly from tumor tissue, and the other two patients with C/C genotype in blood expressed C/T in tumor tissue.

Results: Numbers of patients in each NQO1 genotype were 41 patients for C/C, 83 patients for C/T, and 28 patients for T/T. NQO1 genotypes were classified as three groups, and each genotype had different enzymatic activities; C/C is the wild type with normal activity, C/T is the heterozygous type with decreased activity, and T/T is the homozygous mutation with no enzymatic activity. Thereafter, we analyzed the correlation between NQO1 genotypes and the survival outcome after surgery and postoperative radiation therapy. For the authenticity of genotype from peripheral blood, genotypic analysis was directly from tumor tissue, and the other two patients with C/C genotype in blood expressed C/T in tumor tissue.

T/T genotype (p=0.034). Genotypic analysis from tumor tissue was performed in only eighteen patients. There was accordance in sixteen patients between the genotype from peripheral blood and that directly from tumor tissue, and the other two patients with C/C genotype in blood expressed C/T in tumor tissue.

Conclusions: NQO1 polymorphisms affected on treatment results in NSCLC patients treated with surgery and postoperative radiation therapy. NQO1 could be a useful prognostic factor for NSCLC after radiation therapy, although the further study with more patients and long-term follow-up should be promised.

Session B6: Health Services, Supportive Care & QOL
Tuesday, September 4

B6-01
Health Services, Supportive Care & QOL, Tue, 13:45 - 15:30

Developing clinical guidelines on lung cancer for limited resource settings: an international collaboration supported by the International Atomic Energy Agency (IAEA)

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Introduction: Lung cancer is an increasing problem in developing countries, where access to medical resources may be limited. It is crucial that care in these settings makes most effective and cost-effective use of those resources, based on good evidence. Clinical guideline recommendations from developed countries are not likely to be always (or ever) appropriate and so a different approach is needed.

Methods: An international panel, with a special interest in lung cancer, was invited to a meeting organised by the IAEA in March 2006, at which the main approaches were drafted. Reference was made to recent English language evidence-based clinical guidelines and to other recent systematic reviews, meta-analyses and research. Drafts were then circulated sequentially around the group members, a telephone conference held and a final version approved. We assumed that baseline resources for diagnosis (including CT scanning), radical surgery, radiotherapy (RT) with at least 60Co and 2D planning and IV cisplatin-based combination chemotherapy (CT) would be available. Tables were constructed that showed a baseline standard treatment for different patient groups and the additional benefits, risks and resource use from additional treatment options. Accompanying text summarised the evidence and justification for these options.

Results: Six tables were devised entitled:

1. Options for patients with limited disease SCLC and good prognosis
2. Options for patients with operable NSCLC
3. RT options for patients with medically inoperable NSCLC (Stage I and II)
4. Options for patients with inoperable ‘small’ volume NSCLC (‘Favourable’ Stage III)
5. Options for palliative thoracic RT
6. Options for patients with ‘unfavourable’ Stage III and Stage IV disease and WHO PS 0 or 1.

A comprehensive list of 65 relevant references to current clinical guidelines, systematic reviews and primary research was included.

**Discussion:** We believe that this is an innovative approach to guideline development because it not only summarises the research evidence but makes clear the additional resource use and risks as well as benefits of treatment options. This would enable people to make local decisions about best use of their resources or to develop more sophisticated cost effectiveness models for their local health services. It will also allow those without even the baseline resources to lobby for their provision.

### B6-02 Patterns of lung cancer care in NSW, Australia

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**Background:** Lung cancer is the leading cause of cancer mortality in Australia. However little is known about patient management of this disease in Australia. Previous patterns of care studies showed variability in patient management and a significant proportion of patients not receiving anti-cancer treatment.

**Methods:** Lung cancer patients were prospectively identified from the NSW Central Cancer Registry (CCR) from 1 November 2001 to 31 December 2002. After obtaining patient and/or doctor consent, four separate questionnaires were used to collect information on diagnosis, staging, referrals and treatment. Factors related to patients not receiving treatment were examined using cross-tabulations and logistic regression.

**Results:** There were 2931 potentially eligible patients registered by the CCR of whom 2126 (76%) consented to participate. The study sample comprised 1812 patients (62%) with completed questionnaires. The median age was 71 years with 66% being male. ECOG performance status was rated as good (ECOG 0-2) in 74% of patients. The pathology was non-small cell in 71%, small cell in 16% and not confirmed in 13%.

Eleven percent of patients did not see a lung cancer specialist and 33% received no treatment at initial diagnosis. Treatment utilisation rates were 17% for surgery, 39% for radiotherapy and 30% for chemotherapy. Of the patients who did not receive initial treatment, 6% of patients refused treatment, 28% were deemed unfit for treatment by a surgeon or oncologist and 57% were deemed unsuitable for treatment by another doctor. Female gender, older age, weight loss and poorer performance status were patient factors significantly associated with no treatment.

Patients who did not see a cardiothoracic surgeon or radiation oncologist during the study period were less likely to have treatment. The median survival was 172 days and 2 year crude overall survival was 17%.

**Conclusions:** A significant proportion of patients did not receive treatment for their lung cancer. In most cases this decision was made by a doctor not involved in lung cancer treatment and who was not the best qualified to outline the risks and benefits associated with treatment. Modifying health care provider behaviour is necessary as a major step in improving lung cancer care in NSW.