

## 589 BUILDING PROGNOSTIC MODELS AND SCORES

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Prognostic scores are often constructed to classify patients in prognostic groups thanks to pre-treatment characteristics easily accessible. Once constructed, scores are applied to new patients. Scores are helpful in identifying patients with advanced stage, selecting the appropriate treatment to individual patients, and in stratifying patients in prospective trials.

Models selection is usually based on adequation to initial sample data. Thus prediction on initial data overestimates prediction on new patients.

This difference between predictions, so called model optimism, has to be taken into account when studying predictive ability of models for new patients.

The methodology used to build two prognostic scores is presented. Similar constraints were stated at the beginning ( $\leq 5$  variables in the final score, 3-risk-group score). For follicular lymphomas (Solal-Céligny, 2004), 8 variables were significantly associated with overall survival. The best model including 5 variables was selected on predictive ability. Optimism was corrected using bootstrap. The largest likelihood identified the best score. External validation confirmed the score predictive ability.

For Hodgkin lymphoma (Maucort-Boulch, 2007), 4 variables were significantly associated with 10-year overall survival. The best 3-group score was selected on predictive ability. Optimism was corrected using bootstrap. A first external validation confirmed the better predictive ability in comparison with known scores.

Different measures of prognostic scores predictive ability were proposed (Harrell D, adapted R2, penalized likelihood, Parkes criterion). Those measures could be used for model selection. Their respective properties are still under study. Internal and external validations account for models optimism.

Solal-Céligny P, et al. Follicular lymphoma international prognostic index. *Blood* 2004; 104: 1258-65.

Maucort-Boulch D, et al. Predictive and discriminating three-risk-group prognostic scoring system for staging Hodgkin lymphomas. *Cancer*. 2007; 109: 256-64.

## 590 INTERNET USE BY PATIENTS WITH LYMPHOMA AND THEIR CAREGIVERS

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Patients with cancer and their caregivers frequently seek information about disease management, prognosis, and therapeutic alternatives. The context in which their consume health information has changed dramatically with diffusion of the Internet and advances in telemedicine. At present few data exist of the use of Internet to look for medical information on lymphoma in Spanish language. The aim of our study was to investigate the distribution and patterns of Internet use by patients with lymphoma and her caregivers.

**Patients and Methods:** 1217 subjects (588 patients, 413 relatives, 78 health professionals and 138 others; 476 male and 741 female) have responded a questionnaire about diverse aspects of the use of Internet, in several Haematology Departments of Spanish Hospitals or by "on line" access from the sites [www.aeal.net](http://www.aeal.net), [www.linfomasargentina.org](http://www.linfomasargentina.org) and [www.linfomar.com](http://www.linfomar.com)

**Results:** Seven hundred forty-four (61.1%) subjects use Internet, although only 44% make to obtain data on lymphoma. With respect to the group of patients 65.6% recognize to use Internet, but only the 49.1% do it by questions related to their disease. The main reasons for Internet use are to obtain information about treatments (85.5%) or second opinion medical (5.0%). The 75.0% have been using Internet for more than 3 years; the 52.0% have university studies and the 55.1% have between 31-50 years. Mainly the information search is made in Spanish language and through the Google finder. They consider that information on lymphoma is acceptable (31.5%) or of enough quality (26.6%), trustworthy (33.3%) or of enough reliability (23.8%) and useful (26.9%) or quite useful (25.1%).

**Commentaries:** This study contributes data on the use of Internet in Spanish language by patients with lymphoma and their caregivers. Oncologists should be familiar with this important resource to help the access of affected to appropriate information. The

use of "online" surveys is useful to value some aspects of these diseases in diverse countries.

## 591 ONLINE HEMATOPATHOLOGY, DIAGNOSES AND TRAINING FOR PROMOTION OF HEMATOPATHOLOGY IN CAMBODIA

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**Background:** Cambodia a country of 15m, has no trained hematopathologist. The incidence of hematologic malignancies is similar to the Western World. Our involvement in hematopathology for Cambodia began in 2005 with online diagnoses of bone marrow biopsies (BMB) and aspirates (BMA) as part of a telepathology project, initiated by G.Stauch. Our local partner is a young doctor (SACH) at the Sihanouk Hospital Center of Hope (SHCH), interested in hematopathology.

**Objectives:** To test the reliability of telepathologic diagnoses for hematopathology and to introduce online training as preparation for subsequent conventional training abroad.

**Methods:** "iPath", a software, designed for telepathology (\*) is used for diagnosis and teaching. It's low costs and user friendliness make it suitable for countries with limited resources. The only equipment needed is a microscope with an attached digital camera, and a computer with internet access.

**Procedure:** Slides of BMB and BMA are prepared by a local technician, photographed and submitted to "iPath" by SACH for us (AR, AT, JM, NH.) to evaluate the submitted images. 80 cases have been processed and diagnosed in the period between 2005 and 2007. Recently teleconferences were introduced as preparation for a training period abroad. Diagnostic approach and teaching are adapted to local conditions, focusing on cheap and simple morphologic methods, and emphasizing the need for integration of clinical data for diagnostic considerations to compensate for the lack of sophisticated methods. We also support SACH activities for his academic career to be able to pass on his skills as future teacher of the younger generation.

**Conclusion:** This model serves to evaluate the reliability of telepathology for hematopathology, and the value of online training, as supplement to conventional training to increase the efficiency of conventional training, and reduce its costs. Our preliminary results are encouraging.

\*Brauchli et al. Telemicroscopy by the internet revisited *J. Pathol.* 2002; 196: 238.

## 592 EVALUATION OF BONE MARROW AND SPLEEN INFILTRATION ON THE RISK OF AUTOIMMUNE PHENOMENA GENERATION IN PATIENTS WITH LYMPHOMA

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**Background.** Autoimmune phenomena have been previously reported in association with non-Hodgkin lymphoma (NHL). These studies suggest that the NHL subtypes associated with autoimmune diseases reflect the development of lymphoma during post antigen exposure stages of lymphocyte differentiation consistent with a role of antigen drive in autoimmunity-related lymphomagenesis. However, these reports cannot explain the possible mechanism by the local effect of the tumour in the central tolerance against the generation of auto reactive clones.

**Aim and Methods:** The aim of the present study was to analyse the role of the stage at diagnosis of NHL on the presentation of autoimmune phenomena in patients with Hodgkin lymphoma and NHL. Clinical reports of 167 patients consecutively diagnosed with lymphoma at our institution in the last year were retrospectively reviewed. Autoimmunity was considered positive if the patients had positive autoantibodies (antinuclear, anti-DNA, direct Coombs test, anti-smooth muscle, anti-platelets autoantibodies, anti-cardiolipin, thyroid peroxidase antibodies, anti-EPCR, and anti-IL-1) or a well established autoimmune disease (SLE, TTP or Autoimmune mediated hypothyroidism).

**Results:** The prevalence of autoimmunity in our patients was 11.9%, which is similar to previous reports in the literature. Highest percentages of autoimmune phenomena were detected in patients with diffuse large B-cell lymphoma 5/46 (10.9%), SMZL 4/10 (40%), MALT 1/9 (11.1%) and T-cell lymphoma 5/16 (31%). Interestingly great proportions of patients with autoimmunity 12/20 (60%) were stage IV with bone marrow 12/20 (60%) or spleen 5/20 (25%) infiltration. We hypothesized that infiltration of malignant cells impair negative selection of autorreactive B cell clones in

BM and spleen in advanced stages of disease and contribute to autoimmune phenomena detected in our patients.

### 593 LEVELS OF CIRCULATING DNA IN THE PLASMA AT DIAGNOSIS IN PATIENTS WITH LYMPHOMAS: ASSOCIATIONS WITH CLINICAL CHARACTERISTICS AND PROGNOSIS

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**Background:** Increased levels of circulating nucleic acids (DNA and RNA) with a high fractional concentration of tumor DNA have been observed in the plasma of patients with a variety of human cancers of epithelial origin, and correlated to clinical characteristics and prognosis.

**Methods:** We studied 85 patients with lymphomas [34 pts with Hodgkin lymphoma (HL), 30 pts with diffuse large B cell NHL (DLBCL), 14 pts with follicular, and 6 pts with mantle cell NHL] and 21 healthy individuals. DNA was extracted from plasma collected at diagnosis using the QIAamp DNA Blood MiniKit (Qiagen, UK) and DNA levels were determined using a quantitative PCR for the b-globin gene. Associations with patient characteristics and event-free survival (EFS) were analysed using standard statistics (STATA 10).

**Results:** DNA plasma levels were significantly higher in patients with lymphoma when compared to controls: 75.8 mg/l (mean, range 4-941) vs. 15.7 (mean, range 3-35) (p=0.03), with differences among the different lymphoma types: DLBCL, 130 mg/l; mantle cell NHL, 99 mg/l, follicular NHL, 21 mg/l, HL, 45 mg/l. Advanced stage disease (stage III/IV), presence of B symptoms, LDH levels above normal range, and age >60 years were associated with increased levels of plasma DNA (p=0.016, 0.016, ≤0.0001 and 0.02, respectively). Increased LDH levels were associated with high DNA levels also in the multivariate analysis. In NHL, patients with high risk age-adjusted IPI (2/3) had higher levels of plasma DNA (p=0.001), while in HL no association with the IPS score was observed. Plasma DNA levels above the normal range (>35 mg/l) were associated with an inferior event-free survival (p=0.003), both in patients with HL and DLBCL. The multivariate Cox analysis, stratified for lymphoma type and treatment, including risk factors associated to inferior EFS in the univariate analysis (advanced stage, LDH, and age >60 years), showed that plasma DNA level was an independent prognosticator for inferior EFS (hazard ratio 6.3, 95% CI 1.02-39).

**Conclusion:** Our study suggests that circulating levels of DNA in the plasma may be a new prognostic biomarker in patients with lymphomas.

### 594 NON-HODGKIN'S LYMPHOMA AND DIABETES MELLITUS: RECIPROCAL INFLUENCE ON TREATMENT, COURSE AND OUTCOME

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**Background:** With the increasing prevalence of diabetes mellitus, the rising incidence of non-Hodgkin's lymphoma (NHL) and ageing of the population, the number of patients suffering from both NHL and diabetes is growing. Previous studies have shown that NHL patients with co-morbidity are treated less intensively and have a worse prognosis<sup>1</sup>. Since data for diabetes mellitus as a specific co-morbidity in NHL patients are lacking, we investigated whether diabetes had an influence on treatment and outcome of NHL and vice versa.

**Methods:** All patients diagnosed with NHL between 1995 and 2004 in the area of the population-based Eindhoven Cancer Registry (south eastern Netherlands) are included. Additional information is being collected from medical records for all patients with both NHL and diabetes (n=169) and a random sample NHL patients without diabetes (n=170): functional status, biochemical and body parameters at diagnosis, stage, IPI/FLIPI-score, detailed information on treatment of NHL, toxicity, response to treatment, cause of death and treatment and course of diabetes. Data collection will be completed in 1 month. The independent influence of diabetes on treatment choice, dose-intensity, response rate and survival from NHL as well as the reciprocal influence of NHL and its treatment on the course of diabetes will be investigated.

**Results:** will consist of extensive data-analysis which will give insight in differences in treatment and outcome between the two groups of unselected diabetic and non-diabetic NHL-patients. The results will be presented in Lugano.

**Conclusions:** Literature on the influence of diabetes on treatment and outcome of NHL and vice versa is lacking, whereas knowledge on this topic is highly relevant in the general health care environment for this growing group of patients. With the results of this study, caregivers can anticipate on adverse effects, which hopefully will improve both disease-management and outcome.

<sup>1</sup>. Spronsen van, D.J, Janssen-Heijnen et al., Independent Prognostic effect of co-morbidity in lymphoma patients: Results of the population-based Eindhoven Cancer Registry, *Eur J Cancer* 2005; 41: 1051-57.

### 595 DIAGNOSIS AND TREATMENT OF MALIGNANT LYMPHOMAS IN PREGNANCY AND LACTATION

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**Background:** The lymphomas represent the fourth most frequent malignancy diagnosed during pregnancy, occurring in approximately 1:6000 deliveries. Considerably more often is a diagnosis of the Hodgkin's lymphoma, possibly because of the natural incidence of this disease in the reproductive age of the patients (pts).

**Material and methods:** Since 2001 there were diagnosed 17 pts with a lymphoma during pregnancy or lactation. The median age of the pts was 27 years. The histological types of lymphomas were in most of the cases Hodgkin's lymphoma (n=13), then diffuse large B-cell (n=3) and MALT lymphoma of a eye-lid (n=1). The diagnosis was determined in the 1st (n=2), the 2nd (n=4) and the 3rd trimester (n=4) of pregnancy, at the other 7 pts during lactation (4 of them had a fever or swelling nodes already during the pregnancy). In most of the cases the pts were diagnosed at stage II.

**Results:** 3 of the pts diagnosed during the 1st and the 2nd trimester had an abortion on their own request, 11 pts gave birth to a healthy child naturally (n=7) or by Caesarean section (n=4). In three cases the disease was diagnosed in a critical state of the pts (superior vena cava syndrome or an obstructive ileus), requiring an abortion because of the medical indication of the mother. In the therapeutic plan a histological type of the lymphoma and a clinical stage of the disease were respected. All the pts initiated the treatment after the ending of the pregnancy. The complete remission was achieved at all the pts. 4 of the pts gave birth to a healthy child after the completion of the treatment, the other 2 are currently pregnant.

**Conclusions:** The cases of the diagnosis of the lymphoma during pregnancy are increasing together with the tendency to the family planning in the older age of the mother. However, the pregnancy doesn't affect the overall survival as well as it doesn't influence the prognosis of the disease negatively. The diagnosis of the lymphoma during pregnancy requires a specific and individual attitude while planning the staging examinations and the therapeutic program has to take into account the wish of the patient.

### 596 HETEROGENEITY OF NEW AGGRESSIVE NON-HODGKIN'S LYMPHOMA PATIENTS (NHL) IN TERMS OF QUALITY OF LIFE (QOL) IMPAIRMENT: CORRELATION WITH INTERNATIONAL PROGNOSTIC INDEX (IPI)

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The population of new NHL patients is heterogeneous in terms of clinical parameters and the IPI scoring system is used to make the prognosis. We aimed to study heterogeneity of new NHL patients in terms of their QoL. Based on the grades of QoL impairment there are groups of patients with no, mild (25% decrease from a population norm), moderate (25-50% decrease) severe (50-75% decrease) or critical (>75% decrease) QoL impairment. The identification of the relationship between the grade of QoL impairment and the IPI groups might improve prognostic models in NHL. The purpose of the research was to study the distribution of new NHL patients according to the grades of QoL impairment and to identify their relationship to the IPI groups. 113 new NHL patients (Stage II-IV, mean age 52.5, gender- 58/55) were enrolled. QoL assessment was performed before treatment using SF-36. The method of integral profiles was used to calculate the integral QoL index (IQLI). To determine the relationship between IPI and QoL we examined the distribution of patients according to IPI in QoL impairment groups. The majority of new NHL patients had severe (13.5%) or critical (39.6%) QoL impairment (IOLI - 0.03 and 0.15). 10.8% of patients exhibited mild (IOLI - 0.34) and 16.2% - moderate QoL impairment (IOLI - 0.21). No QoL impairment was observed in 19.8% of patients (IQLI - 0.52). The number of NHL patients who were classified as high-intermediate or high risk according to the IPI within the QoL impairment groups was 31.8% vs 58.3% vs 80.0% vs 81.9 vs 83.0%. Correlation between the ranges of QoL impairment and IPI groups was 0.36 (p=0.001). New aggressive NHL patients are heterogeneous in terms of their QoL impairment. The majority of new NHL patients exhibit significant or critical QoL impairment. The higher the grade of QoL impairment, the higher the risk according to the IPI. With further studies stratification of new NHL patients using IQLI may prove useful in development of improved prognostic models and personalized treatment strategies.