

Press release

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Basic information

Name: Michael Roost Clausen

Email: mrc@clin.au.dk Phone: +4522349670

Department of: Clinical Medicine

Main supervisor: Francesco d'Amore

Title of dissertation: Prognostic factors in diffuse large B-cell lymphoma with focus on anemia, neutropenia and early infections

Date for defence: 29 November at (time of day): 14.00 Place: Aarhus University Hospital, Auditorium C114-101, Entrance C, Palle Juul-Jensens Boulevard 99, 8200 Arhus N

Press release (Danish)

Ph.D.-forsvar af afhandling om prognostiske faktorer hos patienter med lymfekræft

Knap 500 danskere diagnosticeres årligt med diffust storcellet B-celle lymfom (DLBCL) som er den hyppigste form for aggressiv lymfekræft og ubehandlet er sygdommen dødelig indefor måneder. Behandling med immun-kemoterapi +/- stråleterapi, resulterer i 60% af patienterne er i live fem år efter diagnosen. Prognosen er afhængig af flere forhold som f.eks. alder og udbredelse af sygdommen på diagnosetidspunktet, samt genetiske forandringer i kræftcellerne. Det er velbeskrevet i den internationale litteratur. Den prognostiske betydning af blodprocenten på diagnosetidspunktet, graden af hvide blodlegemers fald efter den første kemoterapi samt episoder med infektion er ikke velbelyst. Danske registre gør det muligt at undersøge betydningen af disse forhold og afhandlingen er baseret på analyser af indsamlede data fra Det Danske Lymfomregister, CPR-registret, Landspatientregistret, Patologiregistret og laboratoriedatabaser. Studie 1 og 2 er publiceret og studie 3 er indsendt til et tidskrift.

Studie 1. På baggrund af data fra 3500 patienter diagnosticeret i Danmark i årene 2000-2012, som blev behandlet med helbredende sigte, undersøgte vi betydningen af patientens blodprocent på diagnosetidspunktet. Resultaterne blev sammenlignet med data fra patienter fra Mayo Clinic, Minnesota, USA. Resultaterne viste samstemmende at lavere blodprocent, også nederst i normalområdet, er forbundet med dårlige prognose. Dette til trods for at der blev taget højde for etablerede prognostiske faktorer såsom komorbiditet og alder og særlige sygdomskarakteristika.

I studie 2, undersøgte vi betydningen af kemoterapiens giftvirkning på knoglemarven. Konklusionen fra dette studie er at en grad af giftvirkning synes at være mere fordelagtig end hvis der er et fald i de hvide blodlegemer. Derimod er et kraftig fald i de hvid blodlegemer forbundet med øget risiko for død eller tilbagefald af sygdommen.

Studie 3. Betydningen af indlæggelsekrævende infektion, afhængig af hvornår i behandlingsperioden det optrådte (dag 7-42 vs. dag 100-150), blev vurderet i samme gruppe som studie 1. Vi fandt at infektion optrådte hos 33% og forekomsten var sammenlignelig med andre opgørelser. Uanset timingen var infektion forbundet med en dårligere prognose end ikke at have infektion.

Samlet viser ph.d.-projektet at vi ved sammenkøring af data fra flere danske registre og anvendelse af moderne databearbejdelse og analysemetode kan beskrive både forekomst og prognostisk betydning af observationer og hændelser som ses hos patienter med DLBCL. Vi kan også konkludere at danske patienter er sammenlignelige, hvad angår prognosen, med patienter fra et stort amerikansk center. Sluteligt har projektet ført til etableringen af et samarbejde med Mayo Clinic.

Forsvaret af ph.d.-projektet er offentligt og finder sted den 29. november 2019 i auditorium C114, Aarhus Universitets Sygehus, Auditorium C114-101, Indgang C, Palle Juul-Jensens Boulevard 99, 8200 Arhus N. Titlen på projektet er "Prognostiske faktorer i diffust storcellet B-celle lymfom med fokus på blodmangel, neutropeni og infektioner". Yderligere oplysninger: Ph.d.-studerende Michael R Clausen, e-mail: mrc@clin.au.dk, tlf. +45 2234 9670.

Bedømmelsesudvalg:

Anne-Mette Hvas, professor, PHD, MD. Formand for bedømmelsesudvalget og moderator af forsvaret Klinisk Biokemisk Afdeling, Aarhus Universitetshospital, Danmark

Harald Holte, overlæge, Dr.med, Onkologisk Afdeling, Oslo Universitetshospital, Norge

Kristina Drott, Overlæge, lektor, Ph.D, Hæmatologisk Afdeling, Universitetssygehuset i Lund

Press release (English)

PhD defence

Prognostic factors in diffuse large B-cell lymphoma with focus on anemia, neutropenia and early infections

The project was carried out by Michael R Clausen, who is defending his dissertation on 29 November 2019.

In Denmark, almost 500 patients are annually diagnosed with diffuse large B-cell lymphoma (DLBCL), which is the most common form of aggressive lymphoma and left untreated it is fatal within months. Treatment with immuno-chemotherapy +/- radiation can however lead to long term survival, which is achieved for 60% of patients at five years after diagnosis. The prognosis depends on several factors such as age and stage of the disease at the time of diagnosis, as well as genetic the cancer cells. This is well described in the international literature. However, the prognostic significance of hemoglobin concentration at the time of diagnosis, the degree of neutropenia after the first chemotherapy, and episodes of infection are not well known. Using data from Danish registers we investigated the significance of these conditions and the thesis is based on the analysis and interpretation of data collected from the Danish Lymphoma Registry, the Central Persons Registry, the Danish National Patient Registry, the Pathology Register and laboratory databases. The results are published in two articles and the study 3 is submitted to a journal.

Study 1 is based on data from 3500 patients diagnosed in Denmark in the years 2000-2012 who were treated with curative intent. We investigated the significance of hemoglobin concentration at the time of diagnosis. The results were compared with data from patients from Mayo Clinic, Minnesota, USA. The results showed that lower blood percentage, even at the lower end of normal range, is associated with inferior prognosis compared to the highest quartile. This observation was consistent also when established prognostic factors such as comorbidity, age, and specific disease characteristics were taken into consideration.

In Study 2, we examined the importance of the toxic effect of chemotherapy on the bone marrow in the form of degrees of neutropenia. The conclusion from this study was that a degree of toxicity seems to be associated with a better prognosis compared to no toxicity. In contrast, a decline in neutrophils below $0,5 \times 10^9/l$ is associated with a significant increase in the risk of death or recurrence of DLBCL. Study 3. The significance of infectious episodes requiring hospitalization, depending on when during the treatment period it occurred (day 7-42 vs. day 100-150), was assessed in the same group as study 1. We found that infection occurred in 33% and the incidence was comparable to other studies.

Regardless of the timing, infection was associated with an inferior prognosis compared to not having an infection.

Overall, the PhD project shows that when combining data from several Danish registers and the use of modern data management and analysis, we can describe both the occurrence and prognostic significance of everyday clinical observations and events seen in patients with DLBCL. We can also conclude that Danish patients are comparable in terms of prognosis with patients from a large American center. Finally, the project has led to the establishment of a collaboration with Mayo Clinic.

Assessment committee: Anne-Mette Hvas, professor, PHD, MD. Chairman of the committee and moderator of the defence

Department of Clinical Medicine/Department of Clinical Biochemistry, Aarhus University Hospital, Denmark

Harald Holte, DMSc, MD

Head of Section for Malignant lymphomas, Department of Oncology, Division for Cancer Treatment, Oslo University Hospital, Norway

Kristina Drott, associate professor, PHD, MD

Senior Consultant, Department of Hematology and Transfusion Medicine , Skåne University Hospital, Lund, Sweden

The defence is public and takes place Friday 29 November at 2 pm, Aarhus University Hospital, Auditorium C114-101, Entrance C, Palle Juul-Jensens Boulevard 99, 8200 Arhus N.

For more information, please contact:

PhD student Michael R Clausen, email: mrc@clin.au.dk, Phone +45 2234 9670.

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