Predicting Chemotherapy-Induced Febrile Neutropenia Outcomes in Adult Cancer Patients: An Evidence-Based Prognostic Model

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November 2013
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Abstract

Aims: This thesis explored and examined the clinical factors associated with the outcomes of chemotherapy-induced febrile neutropenia for adult cancer patients and confirms the independent predictive value of these factors. Established as predictors, the factors were used to formulate a multivariable prognostic model to stratify patients according to their risk groupings (high- or low-risk) for adverse outcomes for febrile neutropenia. Newly developed models underwent preliminary validation for their performance as prognostic models for febrile neutropenia outcomes.

Background: Accuracy in risk stratification for cancer patients presenting with chemotherapy-induced febrile neutropenia is of critical importance. Serious morbidity may result when treatment is tailored according to misclassified levels of risk. New predictors and prediction tools used for risk stratification have been reported in the recent years. A systematic review was conducted on this topic as part of the thesis and the findings showed a lack of conclusive information on predictive values for some factors identified as predictors, and limitations in prognostic research studies’ methodologies which affect the internal and external validity of the risk prediction tools.

Methods: Clinical factors identified through the systematic review contributed to the candidate factors investigated. Additional factors were also included based on other primary studies not included in the systematic review. A retrospective review of patients’ medical records was conducted. Tests of association using
univariate analysis were conducted on these variables. Significant variables were tested and adjusted for confounders in a multivariate logistic regression analysis to formulate a multivariable tool for risk stratification of patients presenting with febrile neutropenia.

**Results:** Predictive values for some variables were re-established while some variables failed to demonstrate their predictive values in a univariate analysis. After statistically adjusting to the current factors used in existing prognostic models, a new risk prediction tool was developed predict the risk of adverse outcomes. This tool has been subjected to preliminary validation that confirmed its potential utility. Limitations of the study included single-centre data and the small sample size.

**Conclusions:** Application of a risk prediction tool has its benefits and limitations. However, enhancement of the methodological rigor and comprehensiveness of reporting of results in prognosis research needs to be emphasised for clarity in interpretation and implementation of the studies' findings. Despite the promising initial validation of the tool developed in this thesis, further extensive validation and evaluation of the tool's performance are needed to show the true impact of the tool on clinical practice.
<table>
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<tr>
<th>Abbreviation</th>
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<tr>
<td>ANC</td>
<td>Absolute neutrophil count</td>
</tr>
<tr>
<td>APC</td>
<td>Absolute phagocyte count</td>
</tr>
<tr>
<td>BW</td>
<td>Backward Wald</td>
</tr>
<tr>
<td>CBC</td>
<td>Complete blood cell</td>
</tr>
<tr>
<td>CCF</td>
<td>Congestive cardiac failure</td>
</tr>
<tr>
<td>CDI</td>
<td>Clinically documented infection</td>
</tr>
<tr>
<td>CIN</td>
<td>Chemotherapy-induced neutropenia</td>
</tr>
<tr>
<td>COPD</td>
<td>Chronic obstructive pulmonary disease</td>
</tr>
<tr>
<td>CSF</td>
<td>(Granulocyte) colony stimulating factor</td>
</tr>
<tr>
<td>EBHC</td>
<td>Evidence-based healthcare</td>
</tr>
<tr>
<td>EBM</td>
<td>Evidence-based medicine</td>
</tr>
<tr>
<td>ECOG</td>
<td>Eastern Cooperative Oncology Group</td>
</tr>
<tr>
<td>FN</td>
<td>Febrile neutropenia</td>
</tr>
<tr>
<td>IDSA</td>
<td>Infectious Diseases Society of America</td>
</tr>
<tr>
<td>IHD</td>
<td>Ischaemic heart disease</td>
</tr>
<tr>
<td>IPD</td>
<td>Individual patient data</td>
</tr>
<tr>
<td>JBI</td>
<td>Joanna Briggs Institute</td>
</tr>
<tr>
<td>LB</td>
<td>Literature-based (selected predictors)</td>
</tr>
<tr>
<td>MASTARI</td>
<td>Meta Analysis of Statistics, Assessment and Review Instrument</td>
</tr>
<tr>
<td>MDI</td>
<td>Microbiologically documented infection</td>
</tr>
<tr>
<td>MoAbs</td>
<td>Monoclonal antibodies</td>
</tr>
<tr>
<td>OR</td>
<td>Odds ratio</td>
</tr>
<tr>
<td>PUO</td>
<td>Pyrexia of unknown origin</td>
</tr>
<tr>
<td>ROC</td>
<td>Receiver operating characteristic</td>
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<tr>
<td>WBC</td>
<td>White blood cell</td>
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**Declaration**

I certify that this thesis contains is a record of original work and contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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__________________________________________________________________________  ____________________________________________________________________
Yee Mei, Lee                                            Date
Acknowledgements

With sincere thanks to my supervisors Dr David Tivey and Dr Jared Campbell for their willing support, guidance and encouragement as I worked through the final preparation of this thesis and made it to completion.

My deepest appreciation to Associate Professor Craig Lockwood, Professor Alan Pearson AM and Dr Suzanne Robertson-Malt, for they have never failed to affirm and protect the flickers of curiosity, uncertainties and enthusiasm but encouraged me to let go of the sails, venture and discover.

This work has been possible with the support from the following persons:

Adjunct A/Prof Joe Sim, Chief Executive Officer and Adjunct A/Prof Lee Siu Yin, Director of Nursing, National University Hospital, Singapore for their commendation for the scholarship.

Professor John Wong E.L, Deputy Chief Executive of the NUHS and Director of the National University Cancer Institute, Singapore and Adjunct A/Prof Emily Ang, Deputy Director of Nursing, National University Hospital, Singapore for their continuous support of my aspirations for cancer care.

Dr Chan Yiong Huak, Head, Biostatistics Unit and Dr Ma Thin Mar Win, Yong Loo Lin School of Medicine National University Health System, Singapore, National University Hospital for their continuous advice and statistical support.

Royal Adelaide Hospital staff who have been a tremendous help in my data collection.

Colleagues and patients from NUH, fellow students and “family” from the Joanna Briggs Institute who have extended support, constant words of encouragement and friendship that have made a difference to the journey.

And, my family who believes in me.
Publications

The work of the chapter 3 has been published as follows:
