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

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Table of Contents

List of Tables

List of Figures

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.

List of abbreviations

ANC	-Absolute neutrophil count
APC	- Absolute phagocyte count
BW	- Backward Wald
CBC	- Complete blood cell
CCF	- Congestive cardiac failure
CDI	- Clinically documented infection
CIN	- Chemotherapy-induced neutropenia
COPD	- Chronic obstructive pulmonary disease
CSF	- (Granulocyte) colony stimulating factor
EBHC	- Evidence-based healthcare
EBM	- Evidence-based medicine
ECOG	- Eastern Cooperative Oncology Group
FN	- Febrile neutropenia
IDSA	- Infectious Diseases Society of America
IHD	- Ischaemic heart disease
IPD	- Individual patient data
JBI	- Joanna Briggs Institute
LB	- Literature-based (selected predictors)
MAStARI	- Meta Analysis of Statistics, Assessment and Review Instrument
MDI	- Microbiologically documented infection
MoAbs	- Monoclonal antibodies
OR	- Odds ratio
PUO	- Pyrexia of unknown origin
ROC	- Receiver operating characteristic
WBC	- White blood cell

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.

In addition, I certify that no part of this work will, in the future, be used in a submission for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint-award of this degree.

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* Lee, YM, Lockwood, C. Prognostic factors for risk stratification of adult cancer patients with chemotherapy-induced febrile neutropenia: A systematic review and meta-analysis. Int J Nurs Pract. 2013.

*Lee, YM, Lang, D, Lockwood, C. Prognostic factors for risk stratification of adult cancer patients with chemotherapy-induced febrile neutropenia: A systematic review and meta-analysis JBI Library of Systematic Reviews. 2012;10(40):2593-2657.

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