Health economic impact of use of GCAL® calprotectin immunoassay for early detection of infection in intensive care patients

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INTRODUCTION

Early diagnosis of bacterial infections in critically ill patients is challenging, as the clinical manifestation is non-specific. Neutrophil activation is an early and major response to bacterial infections. Calprotectin constitutes 40-60% of cytosolic protein content in neutrophils and is an early marker for neutrophil activation. Several studies have shown rapid release of calprotectin upon stimulation with endotoxin and/or *E.Coli* (1,2) and the ability of calprotectin to predict bacterial infections before onset of clinical symptoms (3). With early diagnosis of bacterial infections delayed treatment will be avoided as well as deterioration due to severe infection/sepsis.

METHODS

A decision tree model is employed to estimate the impact of calprotectin analysis for early detection of bacterial infections and thus, the earlier start of antibiotic treatment compared to other diagnostic comparators such are white blood cell count (WBC), procalcitonin (PCT), C-reactive protein (CRP), and no testing. The analysis is based on patients admitted to an ICU in a Swedish hospital and a study in which calprotectin predicted bacterial infection 24 hours prior to antibiotic prescription with a sensitivity of 66% and a specificity of 93% at the best cut-off value. Prevalence for infection in the study was 53% [3]. The model allows for different diagnostic outcomes based on correctly and incorrectly diagnosis of bacterial infection and timing of antibiotic treatment: patient survival, length of stay in ICU and in general ward and total costs of treatment during hospital stay.

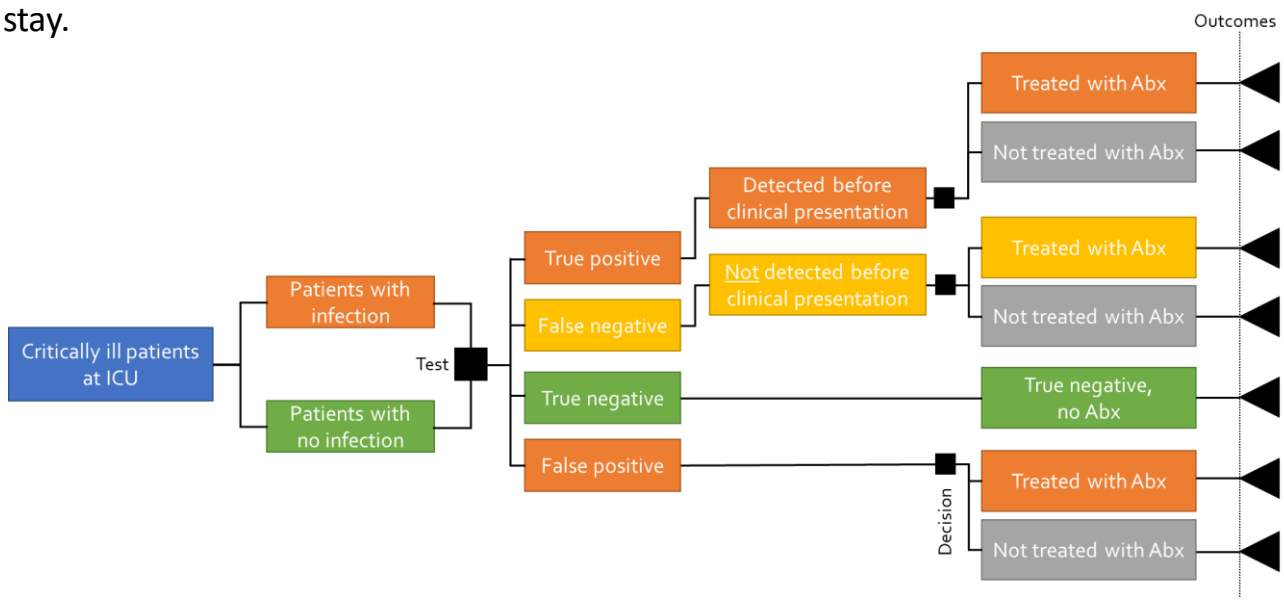

Figure 1. Decision-tree structure with a predictive test

RESULTS

Base-case settings

In the base-case, analysis of calprotectin is employed predictively, differently to the comparators that are employed diagnostically. This means that the proportion of calprotectin tests taken predictively is 100%, while the comparators are set to 0%.

	Δ Total cost (EUR)	Δ Deaths	Δ Mean days ICU	Δ Mean days ward
Calprotectin	Reference	Reference	Reference	Reference
White blood cell count	+12 683	+0.11	+1.27	+7.12
Procalcitonin	+13 756	+0.11	+1.42	+7.27
C-reactive protein	+13 700	+0.11	+1.46	+6.88
No test	+17 522	+0.11	+1.97	+7.82

Table 1. Base-case outcomes (difference compared to calprotectin) per comparator/per patient

The base-case results show that predictively measuring of calprotectin in an ICU setting, using GCAL® calprotectin assay reduces total costs by approximately 13 000 – 18 000 EUR per patient, overall mortality rate by 0.11, and mean length of stay in an ICU and general ward by 1.3 – 2 days and 6.9 – 8 days, respectively.

Sensitivity analyses

Sensitivity analysis was applied to various uncertain parameters in the model. These parameters included: the proportion of predictive tests for comparators where comparators were used predictively in 50% of patients,; the assumption of time to treatment in predictive and diagnostic testing, variation of LoS in ICU and general ward and in-patient costs were cost of in-patient care per day were reduced by 20%. In all sensitivity analyses, calprotectin remains the dominant option when key model inputs are varied.

CONCLUSION

The base-case scenario in presented model identified calprotectin as cost-effective biomarker for a patient cohort presented in a Swedish ICU. Compared to the comparators, PCT, CRP and WBCs calprotectin, analysed by GCAL® Calprotectin Immunoassay was shown to save total costs, reduce the mean duration of in-patient care, and reduce in-hospital mortality in those patients. Although this study focuses on a health economic perspective, the main rationale of analysis of calprotectin is from a clinical perspective, since early diagnosis of severe infections and sepsis reduces both delays in treatment and mortality. From this aspect, our findings support previous ones, where early detection of severe infections and sepsis has both cost-saving and life-saving impact in the ICU setting.

References: 1. Fullerton JN et al., Kinetics of calprotectin, procalcitonin and C-reactive protein in healthy volunteers administered intravenous endotoxin, Crit Care 24 (2020). Abstract No: P474, 2. Lipscey M. et al., The time course of calprotectin liberation from human neutrophil granulocytes after Escherichia coli and endotoxin challenge. Innate Immun. 2019 Aug;25(6):369-373, 3.Jonsson, N. et al., Calprotectin as an early biomarker of bacterial infections in critically ill patients: an exploratory cohort assessment. Crit Care Resusc. 2017 19, 205-213.

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