CRITICAL CARE

LETTER

# Limitation of (1→3)-β-D-glucan monitoring in major elective surgery involving cardiopulmonary bypass

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Measuring (1→3)-β-D-glucan has recently been advocated for detection of invasive candidiasis. Our data indicate that the rate of false positive results is potentially high in some patient collectives of risk; for example, after cardiac artery bypass grafting (CABG).

The recently published guidelines from the Surviving Sepsis Campaign recommend the use of (1→3)-β-D-glucan as a surrogate for invasive candidiasis [1]. Fungal infections are increasing, are underestimated by conventional culture, and are associated with high mortality [2,3]. Testing for fungal wall constituents can detect candidiasis early, but its additional value in critically ill patients remains unclear [4]. We investigated (1→3)-β-D-glucan levels in patients with sepsis and compare the values with those of postoperative patients after CABG, reflecting a well-defined ICU cohort.

After institutional approval by Local Ethics Committee Jena, 21 patients (aged ≥18 years) with sepsis, severe sepsis or septic shock according to American College of Chest Physicians/Society of Critical Care Medicine criteria, 23 patients after onpump CABG as well as 21 healthy controls were enrolled. All patients or legal surrogates gave informed consent. Patients' characteristics are presented in Table 1. Blood sampling was performed in patients on the day of diagnosis (sepsis) or on the first postoperative day (CABG). The measurement of (1→3)-β-D-glucan was performed by WAKO Inc. (Osaka, Japan).

We found increased (1→3)-β-D-glucan levels in patients with sepsis compared with healthy controls (Figure 1), but patients after CABG exhibited the highest median (1→3)-β-D-glucan values; none developed signs of invasive candidiasis and the median ICU length of stay was 1 day. Eleven of 18 (61%) patients with sepsis reached (1→3)-β-D-glucan levels above the upper limit of normal (11 pg/ml). An incidence rate of 61% for invasive candidiasis appears very high [2], suggesting that cutoff values in the ICU setting where translocation might occur warrant reappraisal. Similarly, eight out of 18 (44%) patients after CABG presented elevated levels.

Since the highest levels of (1→3)-β-D-glucan were found in CABG patients after onpump surgery, we assume – similarly to patients undergoing haemodialysis [5] – that (1→3)-β-D-glucan might have derived from membranes during onpump surgery rather than from infection or translocation. Since elevated (1→3)-β-D-glucan levels in

**Table 1. Characteristics of the patients**

| | Sepsis | CABG | *P* value |
|---|---|---|---|
| Age (years) | 72 (56 to 78) | 60 (54 to 68) | <0.05 |
| APACHE II score | 19 (17 to 25) | 7 (6 to 11) | <0.001 |
| SOFA score | 9 (7 to 12) | 4 (2 to 5) | <0.001 |
| C-reactive protein (mg/l) | 162 (127 to 200) | 59 (43 to 96) | <0.001 |
| ICU LOS (days) | 23 (12 to 39) | 1 (1 to 1) | <0.001 |
| Hospital LOS (days) | 42 (23 to 62) | 11 (10 to 13) | <0.001 |

Data presented as median (interquartile range). APACHE, Acute Physiology and Chronic Health Evaluation; CABG, cardiac artery bypass grafting; LOS, length of stay; SOFA, Sequential Organ Failure Assessment.

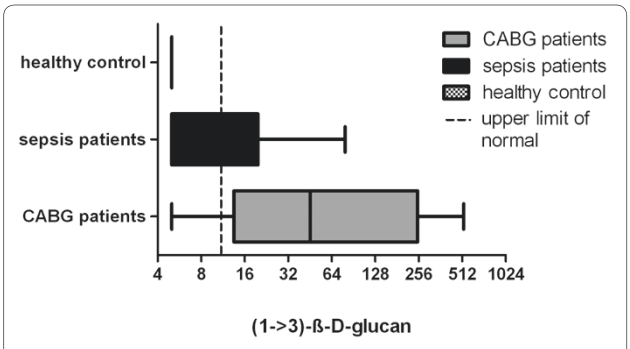


**Figure 1. (1→3)-β-D-glucan levels in critically ill patients.** Concentration of (1→3)-β-D-glucan levels in healthy controls, patients with sepsis and patients after cardiac artery bypass grafting. Dotted line represents upper limit of normal (11 pg/ml). CABG, cardiac artery bypass grafting.

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these patients do not reflect invasive candidiasis (data not shown), elevated (1→3)-β-D-glucan levels need careful interpretation in patients treated with artificial membranes. Longitudinal measurements of (1→3)-β-D-glucans in critically ill patients might be more useful as a surrogate for invasive candidiasis. A contribution of fungal pathogen-associated molecular patterns from the circuit triggering at least in part the systemic inflammatory response to cardiopulmonary bypass has yet to be tested.

**Abbreviations**
CABG, cardiac artery bypass grafting.

**Competing interests**
The authors declare that they have no competing interests.

**Authors' contributions**
GPO and BS designed the study and wrote the first draft of the manuscript. IDJ, KL and BH were involved in data analysis and interpretation. MB was involved in supervision, data analysis and its interpretation. All authors read and approved the final draft of the manuscript.

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