SMARTDIAGNOS – next generation molecular sepsis diagnosis technology for whole blood samples

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Objectives

The aim of the present performance evaluation was to investigate the potential of the LAB system with newly developed molecular hybcell technology on collected patient blood samples in three clinical microbiology labs in Sweden, the Czech Republic and Austria.

Background

The objective of the EU Horizon 2020 project SMARTDIAGNOS was to develop a molecular PCR-based technology for detection and identification of sepsis-causing pathogens directly in whole blood.

Methods

- Dilution series of bacterial and fungal reference isolates
- 403 freshly collected whole blood samples
- Manual DNA extraction with the GINA kit (Cube Dx)
- LAB system (Cube Dx):
  - -Broad-range PCR for detection of neg/pos samples
  - -"Compact sequencing" in a hybcell of positive samples (fig 1) on the hyborg (fig 2)
- Test covers 101 molecular targets including bacterial-, resistance- and fungal genes
- Performance characteristics were evaluated: time-to-result, diagnostic sensitivity, specificity, accuracy, diagnostic odds ratio, positivity rate, coverage rates
- Operational characteristics were evaluated: total hands-on-time and simplicity. End user experience was considered by interviews.
- Conventional blood culture was used as reference.
- SeptiFast (Roche) was used in parallel for comparison of results on 51 blood samples

Figure 1. Hybcell (Cube Dx)

Figure 2. Hyborg (Cube Dx)

Table 1

Results from data analysis of raw data		
	Blood culture positive (reference)	Blood culture negative (reference)
LAB positive	True positive: 16 (5%)	False positive: 155 (44%)
LAB negative	False negative: 20 (6%)	True negative:157 (45%)
Results after extended data analysis and fine tuning of reporting		
	Blood culture positive (reference)	Blood culture negative (reference)
LAB positive	True positive: 28 (8%)	False positive: 5 (1%)
LAB negative	False negative: 10 (3%)	True negative: 309 (88%)

Results

In total, 36/403 (9%) were blood culture positive. A positive PCR-result was obtained in 171/403 (42%). True and false positive and negative rates were calculated before (n=348) and after (n=352) extended data analysis of the raw data; adjustment of protocol and threshold, elimination of skin flora contaminants and clinical credibility of discrepant results (Table 1). Sensitivity was then 70% and specificity 99%. In total, 96% of the samples were correctly classified by the LAB system. Accordance of SeptiFast with blood culture was 83% compared to 86% accordance of the LAB system for the same samples.

Conclusions

The LAB system performs well in detecting pathogens directly in blood and covers at least 80-85% of the microorganisms causing severe infections in Europe. The technologies developed during the SMARTDIAGNOS project include and identify a wide range of pathogens. The system is easy to use with a 4 h response time for a single sample. Remote access of the LAB instrument allows timely technical support.

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