Performance of Galactomannan-Antigen-Test, Aspergillus Lateral-Flow-Device-Test, 1,3-Beta-D-Glucan, Conventional Culture and Aspergillus-PCR for Diagnosis of Invasive Pulmonary Aspergillosis in Bronchoalveolar Lavage: A Cohort Study

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Studie Nummer 8

Purpose: The aim of this study was to compare the performance of galactomannan-antigen-test (GM), conventional culture, *Aspergillus* lateral-flow-device test (LFD), 1,3-Beta-D-Glucan (BDG) and *Aspergillus* polymerase-chain-reaction (PCR) assay in bronchoalveolar lavage (BAL) fluid specimens from immunocompromised patients regarding early detection of invasive pulmonary aspergillosis (IPA).

Methods: 68 BAL samples from 68 patients (64 from Graz, 4 from Mannheim) were included between December 2012 and May 2013 at two university hospitals in Austria and Germany. 3 patients had proven IPA, 7 probable, 17 possible and 41 patients no IPA. Diagnostic accuracy of all 5 methods (BDG in samples from Graz only) for probable/proven IPA was evaluated. For IPA grading fungal cultures as well as BAL GM (cut-off 1.0 U/L) were used.

Results: Sensitivity, specificity, positive (PPV) and negative predictive value (NPV) as well as diagnostic odds ratio (DOR) of all 5 tests for probable/proven IPA are depicted in the table. Combination of GM [>1.0 optical density (OD)] with LFD increased the sensitivity to 90% while combination of GM (>1.0 OD) with PCR resulted in a 100% sensitivity (specificity for propable/proven IPA 95%, specificity after exclusion of possible IPA 98%). One patient was diagnosed with invasive fusariosis. This particular patient had only positive culture and BDG (389pg/mL). Details are displayed in table 1.

Conclusion: We evaluated established and novel diagnostic methods for aspergillosis and found that *Aspergillus* PCR, LFD and GM are useful methods for diagnosis of IPA in BAL samples. In particular combination of GM and PCR or - if PCR is not available - LFD seems promising.

	Sensitivity	Specificity	PPV	NPV	DOR/95% confidence interval
GM >1.0 U/L	70%	98%	88%	93% (95%)	93.3/8.5-1030 (133/12.1-1459)
GM >0.5 U/L	80%	98% (90%)	89% (57%)	95% (96%)	160/12.9-1984 (34.7/5.9-203)
Mycological Culture	50%	95% (97%)	71%	89% (92%)	19.5/3-129 (28/4.3-183)
BDG >80 pg/mL	86%	75% (67%)	38% (24%)	97%	18/1.9-168 (12/1.3-107)
BDG >200 pg/mL	71%	88% (75%)	50% (26%)	95% (96%)	17.5/2.7-116 (7.7/1.3-44.1)
LFD	80%	95% (84%)	80% (47%)	95% (96%)	78/9.5-639 (21.8/4-120)
PCR	70%	100% (96%)	100% (78%)	93% (95%)	161/7.5-3445 (60.7/8.6-429)

Table 1 Diagnostic performance of BAL GM, culture, BDG, LFD and PCR for probable and proven IPA versus no IPA and no IPA plus possible IPA (in brackets if differing). Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic odds ratio (DOR) displayed

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