CandiDia-Antibody – Selected References

Published Articles and Guidelines

Author(s)	Year	Title	Journal
Ardizzoni et al	2014	AN ANTIBODY REACTIVITY-BASED ASSAY FOR DIAGNOSIS OF INVASIVE CANDIDIASIS USING PROTEIN ARRAY	INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY
The increased incidence of invasive candidiasis and of patients at risk requires early diagnosis and treatment to improve prognosis and survival. The aim of this study was to set up a ten-protein array- based immunoassay to assess the IgG antibody responses against ten well-known immunogenic C. albicans proteins (Bgl2, Enol, Pgkl, Pdcll, Fbal, Adhl, Als3, Hwpl, Hsp90 and Grp2) in 51 patients with invasive candidiasis (IC) and in 38 culture-negative controls (non-IC). Antibody levels were higher against Bg12, Enol, Pgkl, Als3, Hwpl and Grp2, than against Adhl, Pdcll, Fbal and Hsp90, irrespectively of the patient group considered. Moreover, the IgG levels against Bg12, Enol, Pgkl and Grp2 were significantly higher in IC than in non-IC patients. Furthermore, the ROC curves generated by the analysis of the antibody responses against Bg12, Grp2 and Pgkl displayed AVC values above 0.7, thus discriminating IC and non-IC patients. According to these results, the employment of the microarray immunoassay (a rapid, sensitive and multiparametric system), in parallel with conventional diagnostics, can help to spot IC patients. This ultimately will allow to initiate an early, focused and optimized antifungal therapy.			
Aubert et al	1996	Characterization of specific anti-Candida IgM, IgA and IgE: diagnostic value in deep-seated infections	Mycoses
The proposed serological diagnosis of systemic Candida infections is based on a microplate immunocapture technique detecting IgM, IgA and IgE anti-Candzda antibodies. Activity is revealed with a suspension of human erythrocytes sensitized with somatic antigen of Candida albzcans, and is quantified on an automated plate reader. The sera were obtained from patients with deep- seated (n = 56) and superficial (n = 193) candidosis. We compared this immunological method with a combination of indirect immunofluorescence and co-immunoelectrodiffusion. The immunocapture method was more sensitive (80.4% vs. 48.2% with indirect immunofluorescence and 58.9% with co-immunoelectrodiffusion), and often provided the diagnosis at an earlier stage, with clear therapeutic advantages. The IgA isotype was a particularly valuable marker of deep-seated Candida infections.			
Clancy et al	2008	Immunoglobulin G Responses to a Panel of Candida albicans Antigens as Accurate and Early Markers for the Presence of Systemic Candidiasis	JOURNAL OF CLINICAL MICROBIOLOGY
Despite shortcomings, cultures of blood and sterile sites remain the “gold standard” for diagnosing systemic candidiasis. Alternative diagnostic markers, including antibody detection, have been developed, but none are widely accepted. In this study, we used an enzyme-linked immunosorbent assay to measure serum antibody responses against 15 recombinant Candida albicans antigens among 60 patients with systemic candidiasis due to various Candida spp. and 24 uninfected controls. Mean immunoglobulin G (IgG) responses against all 15 antigens were significantly higher among patients with systemic candidiasis than among controls, whereas IgM responses were higher against only seven antigens. Using discriminant analysis that included IgG responses against the 15 antigens, we derived a mathematical prediction model that identified patients with systemic candidiasis with an error rate of 3.7%, a sensitivity of 96.6%, and a specificity of 95.6%. Furthermore, a prediction model using a subset of four antigens (SET1, ENO1, PGK1-2, and MUC1-2) identified through backward elimination and canonical correlation analyses performed as accurately as the full panel. Using the simplified model, we predicted systemic candidiasis in a separate test sample of 32 patients and controls with 100% sensitivity and 87.5% specificity. We also demonstrated that IgG titers against each of the four antigens included in the prediction model were significantly higher in convalescent-phase sera than in paired acute- phase sera. Taken together, our findings suggest that IgG responses against a panel of candidal antigens might represent an accurate and early marker of systemic candidiasis, a hypothesis that should be tested in future trials.			
Martinez-Jimenez et al	2014	Potential role of Candida albicans germ tube antibody in the diagnosis of deep-seated candidemia	Medical Mycology
Patients with candidemia may have transient or catheter-related infections without involvement of deep tissues or deep-seated candidiasis. Clinical differentiation of these entities may not be evident with conventional microbiological and imaging methods. Our aim was to determine if the detection of Candida albicans germ tube–specific antibody (CAGTA) in patients with candidemia was related to the extent of the disease. This study was conducted from 2003 to 2012 with 50 patients diagnosed as having candidemia, that is, 29 with deep-seated candidiasis and 21 with non-deep-seated candidiasis. The most common species recovered from samples obtained from these patients were C. albicans, 40%; C. tropicalis, 20%; C. parapsilosis, 18%; and C. glabrata, 12%. Serum samples were processed according to the manufacturer’s recommendations (Vircell Microbiologist S.L., Granada, Spain). The CAGTA tests were positive in 1/21 non-deep-seated candidemias (DSCs; 4.76%) and 20/29 DSCs (68.96%; $P < 0.01$). Accordingly, the values for specificity and positive predictive values of CAGTA for identifying DSC were 95%. We concluded that the presence of a positive CAGTA test in a sample from a patient with candidemia suggests deep-seated candidiasis. Extension screening studies should be considered and origins other than catheters should be searched. Prospective studies are needed to determine the clinical implications of this finding and its potential use in defining the optimal duration of therapy.			
Pitarch et al	2006	Decoding Serological Response to Candida Cell Wall Immunome into Novel Diagnostic, Prognostic, and Therapeutic Candidates for Systemic Candidiasis by Proteomic and Bioinformatic Analyses	Molecular & Cellular Proteomics
Multivariate logistic regression models demonstrated that high levels of antibodies against glucan 1,3-□-glucosidase (Bgl2p) and the anti- wall phosphoglycerate kinase antibody seropositivity were the only independent predictors of SC. Receiver operating characteristic curve analysis revealed no differ- ence between their combined evaluation and measure- ment of anti-Bgl2p antibodies alone. In a logistic regres- sion model adjusted for known prognostic factors for mortality, SC patients with high anti-Bgl2p antibody levels or a positive anti-wall enolase antibody status, which cor- related with each other, had a reduced 2-month risk of death. After controlling for each other, only the seropos- itivity for anti-wall enolase antibodies was an independent predictor of a lower risk of fatality, supporting that these mediated the protective effect. No association between serum anti-cytoplasmic enolase antibody levels and out- comes was established, suggesting a specific mechanism of enolase processing during wall biogenesis. We con- clude that serum anti-Bgl2p antibodies are a novel accurate diagnostic biomarker for SC and that, at high levels, they may provide protection by modulating the anti-wall enolase antibody response. Furthermore serum anti-wall enolase antibodies are a new prognostic indicator for SC and confer protection against it. Bgl2p and wall-associ- ated enolase could be valuable candidates for future vac- cine development.			
Pitarch et al	2011	Prediction of the Clinical Outcome in Invasive Candidiasis Patients Based on Molecular Fingerprints of Five Anti-Candida Antibodies in Serum	Molecular & Cellular Proteomics
Multivariate logistic-regression and receiver-operating-characteristic curve analyses demonstrated that the ICPS was able to accurately discriminate IC patients at high risk for death from those at low risk and outperformed conventional IC prognostic factors. Further validation of the five-IgG anti- body-reactivity signature on a multiplexed immunoassay supported the serological proteome analysis results. The five IgG antibodies incorporated in the ICPS made bio- logic sense and were associated either with good-prog- nosis and protective patterns (those to Met6p, Hsp90p, and Pgk1p, putative Candida virulence factors and			

anti- apoptotic mediators) or with poor-prognosis and risk pat- terns (those to Ssb1p and Gap1p/Tdh3p, potential Can- dida proapoptotic mediators). We conclude that the ICPS, with additional refinement in future larger prospective cohorts, could be applicable to reliably predict patient clinical-outcome for individualized therapy of IC. Our data further provide insights into molecular mechanisms that may influence clinical outcome in IC and uncover poten- tial targets for vaccine design and immunotherapy against IC.

Quindos et al	2004	Is there a role for antibody testing in the diagnosis of invasive candidiasis?	Rev Iberoam Micol

During the last decades, the use of antibody tests for the diagnosis of invasive mycoses has declined as a consequence of the general belief that they are insensitive and non-specific. However, there is a clear evidence that antibodies can be detected in highly immunodeficient patients (such as bone marrow transplant recipients), and that those antibodies are useful for the diagnosis. Antibody tests are currently in use as diagnostic tools for some primary mycoses, such as the endemic mycoses, aspergilloma, allergic broncho- pulmonary aspergilosis and sporothrichosis. For invasive candidiasis, diagnostic methods must differentiate Candida colonization of mucous membranes or superficial infection from tissue invasion by this microorganism. Substantial progress has been made in diagnosis of invasive candidiasis with the development of a variety of methods for the detection of antibodies and antigens. However, no single test has found widespread clinical use and there is a consensus that diagnosis based on a single specimen lacks sensitivity. It is necessary to test sequential samples taken while the patient is at greatest risk for developing invasive candidiasis to optimize the diagnosis. Results obtained from a panel of diagnostic tests in association with clinical aspects will likely be the most useful strategy for early diagnosis and therapy.

Thornton	2013	Lateral-Flow Device for Diagnosis of Fungal Infection	Curr Fungal Infect Rep

Invasive aspergillosis (IA) is a life-threatening complication of haematological malignancy and haemato- poietic stem cell transplantation caused by the ubiq- uitous fungus Aspergillus. Current diagnosis of IA is multifaceted relying on data from clinical, radiological, and microbiologi- cal sources. The detection of Aspergillus biomarkers provides strategies both to pre-empt and to exclude disease, but the choice of biomarker assays is limited, requiring specialist equip- ment and training. This review examines recent advan- ces in the accurate diagnosis of IA through the development of an Aspergillus lateral-flow device (LFD) incorporating a monoclonal antibody, JF5, which detects an antigenic marker of active infection. Recent trials using bronchoalveolar lavage fluids and serum samples from humans and from animal models of disease, have demonstrated the utility of the LFD as a rapid and user-friendly adjunct test for the quick and accurate diagnosis of pulmonary infections.

Wei et al	2019	Diagnostic accuracy of Candida albicans germ tube antibody for invasive candidiasis: systematic review and meta-analysis	Diagnostic Microbiology and Infectious Disease

Candida albicans germ tube antibody (CAGTA) may be helpful as a marker for the diagnosis of invasive candidiasis (IC). However, the performance has been variable. We conducted a meta-analysis to assess the diagnostic accuracy of this assay for diagnosing IC. We searched MEDLINE, EMBASE, Cochrane Collabo- ration databases, reference lists of retrieved studies, and review articles. The sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, diag- nostic odds ratio, and a summary receiver-operating characteristic curve of CAGTA for diagnosing IC were pooled using meta-analysis. A total of 976 patients (262 with proven or probable IC), included in 7 studies, were analyzed. The pooled sensitivity, specificity, positive and negative likelihood ratios, and diagnostic odds ratios and area under the curve were 66% (95% confidence interval [95% CI], 59% to 73%), 76% (95% CI, 58% to 88%), 2.8 (95% CI, 1.5 to 5.8), 0.44 (95% CI, 0.34 to 0.57), 6 (95% CI, 3 to 5), and 0.68 (95% CI, 0.64 to 0.72), respectively. Heterogeneity of specificity was significant. The diagnostic accuracy of the CAGTA assay is moderate for IC. Since the CAGTA assay is not absolutely sensitive and specific for IC, the CAGTA results should be interpreted in parallel with other biomarkers and clinical findings.

Gutirrez et al	1993	Circulating Candida Antigens and Antibodies: Useful Markers ofCandidemia	JOURNAL OF CLINICAL MICROBIOLOGY

To investigate the utility of the 48-kDa antigen from Candida albicans in its commercial form (Directigen; Becton Dickinson) and three other serodiagnostic methods (detection of one antigen by Pastorex Candida [SanofiDiagnosticsPasteur]anddetectionofimmunoglobulinG [IgG1andIgMantibodiestoC.albicans blas- toconidia [bioMerieuxl) for diagnosis of invasive Candida infection, we conducted a prospective clinical trial among 10 patients with candidemia (group 1), 30 patients colonized by C. albicans (group 2), 20 patients with bacteremia (group 3), and 20 subjects without clinical or microbiological evidence of infection. The Directigen system was positive for at least one serum sample each from eight patients in group 1. In groups 2, 3, and 4, itwas positive for only three patients. There was no reaction to the Pastorex system in any of the patients infected with or colonized by C. albicans or in the non-Candida-carrying controls. The IgG antibody concentration oscillated between 100 and 800 (mean, 510 ± 268) IU/ml for the patients in group 1. In this group, eight patients had IgG antibody levels of >400 IU/ml. The percentages of persons with IgG antibody levels of >400 IU/ml in groups 2, 3, and 4 were 43.3, 0, and 0, respectively. Specific IgM antibody was present inalgroup 1patientsbutnotinthoseingroups2,3,and 4.The sensitivityand specificityoftheDirectigen test were 65 and 97.1%, respectively. For the Pastorex test, the sensitivity was 0%Y. The sensitivity of IgG antibodies was 80%, with a specificity of 81.4%, while the IgM antibodies were 100%v specific and sensitive. Both the positive and negative predictive values of specific IgM antibodies appeared to be superior to those of theother- threetests.

Takaki et al	1996	Detection of Candida Antigen and Antibody in Serum from Patients with Invasive Can- didiasis	International Journal of Infectious Diseases

To compare the sensitivity and specificity of three different assays for diagnosis of invasive candidiasis. A passive hemagglutination assay (PHA), counter- immunoelectrophoresis assay (CIE), and Cand-tee were used to test sera from 125 patients with hematologic malignancies and 65 other hospitalized patients. The former group included 15 patients with invasive candidiasis, 38 patients with Candida colonization, and 72 patients without candidiasis. Sensitivity/spec- ificity of PHA, CIE, and Cand-tee were 87%/85%, 67%/98%, and 33%/97%, respectively. The mea- surement of antibody in paired sera, by PHA, was sensitive and specific; however, increased antibody titers usually occurred late in the disease. The combination of PHA and CIE, with a sensi- tivity of 67% and specificity of 98%, appeared to be the best assays for detection of invasive candidiasis in this cohort. The Cand-tee assay for Candida antigen had poor sensitivity for diagnosis of infection.

Mattsby-Baltzer et al	2015	IgG1 anti-cell wall and IgG2 anti-phosphopeptidomannan antibodies in the diagnosis of invasive candidiasis and heavy Candida colonization	Medical Mycology

We conducted a retrospective study to evaluate the usefulness of immunoglobulin G (IgG) subclasses against Candida cell wall fragments (CW) and phospho- peptidomannan (PPM) for the diagnosis of invasive candidiasis (IC). We analyzed 54 patients with IC (n = 19), Candida heavy colonization (HC; n = 16), and controls (no IC or HC, n = 19). In nonneutropenic patients (n = 47), the sensitivity and specificity values of IgG1 anti-CW and IgG2 anti-PPM in IC were 88%, 59%, and 88%, 94%, respectively. The areas under the receiver operating characteristic curves were 0.69 (0.51–0.88) and 0.901 (0.78–1.02), respectively. IgG1 mean values (arbitrary units) and 95% confidence interval were 46 (20–71), 42 (−0.38 to 84) and 20 (8.3–32) in IC, HC, and in controls, respectively, and discriminated IC but not HC from controls (P = .032, and P = .77, respectively). IgG2 mean values were 26 (9.2–42), 19 (4.4–33), and 3.2 (0.28–6.6) in IC, HC, and in controls, respectively, and discriminated both IC and HC from controls (P < .0001 and P = .035, respectively) but did not separate IC from HC (P = .2). IgG2 showed positivity as early as one day after the IC diagnosis. Antibodies were detected in only two out of a total of seven neutropenic patients. For both IC and HC patients, the diagnostic performance of IgG2 anti-PPM was better than the one of IgG1 anti-CW. In nonneutropenic patients, IgG2 anti-PPM accu- rately identifiednot only IC patients but also HC patients at high risk for IC. This marker may help clinicians in the initiation of early preemptive therapy.

Lain et al	2007	Diagnosis of invasive candidiasis by enzyme-linked immunosorbent assay using the N- terminal fragment of Candida albicans hyphal wall protein 1	BMC Microbiology

The diagnosis of invasive candidiasis is difficult because there are no specific clinical manifestations of the disease and colonization and infection are difficult to distinguish. In the last decade, much effort has been made to develop reliable tests for rapid diagnosis of invasive candidiasis, but none of them have found widespread clinical use. Antibodies against a recombinant N-terminal fragment of the Candida albicans germ tube- specific antigen hyphal wall protein 1

		(Hwp1) generated in Escherichia coli were detected by both immunoblotting and ELISA tests in a group of 36 hematological or Intensive Care Unit patients with invasive candidiasis and in a group of 45 control patients at high risk for the mycosis who did not have clinical or microbiological data to document invasive candidiasis. Results were compared with an immunofluorescence test to detect antibodies to C. albicans germ tubes (CAGT). The sensitivity, specificity, positive and negative predictive values of a diagnostic test based on the detection of antibodies against the N-terminal fragment of Hwp1 by immunoblotting were 27.8 %, 95.6 %, 83.3 % and 62.3 %, respectively. Detection of antibodies to the N-terminal fragment of Hwp1 by ELISA increased the sensitivity (88.9 %) and the negative predictive value (90.2 %) but slightly decreased the specificity (82.6 %) and positive predictive values (80 %). The kinetics of antibody response to the N-terminal fragment of Hwp1 by ELISA was very similar to that observed by detecting antibodies to CAGT. An ELISA test to detect antibodies against a recombinant N-terminal fragment of the C. albicans germ tube cell wall antigen Hwp1 allows the diagnosis of invasive candidiasis with similar results to those obtained by detecting antibodies to CAGT but without the need of treating the sera to adsorb the antibodies against the cell wall surface of the blastospore
Clancy & Nguyen	2018	Diagnosing Invasive Candidiasis	J. Clin. Microbiol
		Cultures are negative in ~50% of invasive candidiasis. Data are emerging for the performance of non-culture tests like mannan/anti-mannan, Candida albicans germ tube antibody, 1,3-β-D-glucan, polymerase chain reaction, and the T2Candida panel in diagnosing both candidemia and deep-seated candidiasis. In most settings, positive predictive values of non-culture test are low, and negative predictive values are high. For tests to be useful, clinicians must understand the pre-test likelihood of invasive candidiasis and test performance for the most common disease manifestation in a given patient. This paper reviews non-culture Candida diagnostics, and discusses how they might be used effectively in patient care.
Lain et al	2007	Evaluation of a Novel Enzyme-Linked Immunosorbent Assay To Detect Immunoglobulin G Antibody to Enolase for Serodiagnosis of Invasive Candidiasis	CLINICAL AND VACCINE IMMUNOLOGY
		The performance of a new test to detect antibodies to Candida albicans recombinant enolase was investigated in 47 immunocompromised and 51 immunocompetent patients. The sensitivity, specificity, and positive and negative predictive values of the test for the diagnosis of invasive candidiasis were 81.0, 83.9, 79.1, and 85.5%, respectively.
Martinez-Jimenez et al	2015	Combination of Candida biomarkers in patients receiving empirical antifungal therapy in a Spanish tertiary hospital: a potential role in reducing the duration of treatment	J Antimicrob Chemother
		Initiation of empirical antifungal therapy for invasive candidiasis (IC) is usually based on clinical suspicion. Serological biomarkers have not yet been studied as a means of ruling out IC. We evaluated the poten- tial role of two combined biomarkers in stopping unnecessary antifungals in patients at risk of IC in the ICU and in other wards. This was a prospective observational study including adults starting empirical antifungal treatment for suspected IC, at Gregorio Marañ ́o ́n Hospital, Madrid (Spain). Patients were stratified according to admission department (ICU or other wards) and final diagnosis (no IC or proven or probable IC). Type of candidiasis (candi- daemia or deep-seated candidiasis) was also considered. The Candida albicans germ tube antibody (CAGTA) test and the b-D-glucan (BDG) test were performed on serum samples collected by venepuncture on days 0, 3 and 5 after starting empirical antifungal therapy. Sixty-three ICU patients and 37 non-ICU patients were included. High-risk gastrointestinal surgery and sepsis in non-surgical patients were the main indications for empirical treatment (30% each). Patients had no IC (58%), proven IC (30%) or probable IC (12%). Overall, sensitivity and negative predictive value of the combination of both the CAGTA test and the BDG test were 97% for the entire population. The best performance was observed in ICU patients (sensitivity and negative predictive value of 100%). Among patients without IC, all biomarkers were negative in 31 patients. Serial determination of CAGTA/BDG during empirical antifungal therapy has a high sensitivity and negative predictive value. If properly confirmed, this strategy could be used to discontinue antifungal treatment in at least 31% of patients as a complementary tool in antifungal stewardship programmes.
Martinez-Jimenez et al	2015	Candida biomarkers in patients with candidaemia and bacteraemia	J Antimicrob Chemother
		Microbiological strategies are necessary to help clinicians discontinue empirical antifungal therapy in patients with suspected invasive candidiasis. Culture methods and biomarkers each show low sensitivity. We analysed the value of combining different biomarkers as a decision-making tool for discontinuing empirical antifungal treatment. We studied stored serum samples from 31 patients with candidaemia (Candida albicans 40%, Candida tropicalis 20%, Candida parapsilosis 18%, Candida glabrata 12% and other 10%) and 50 patients with bacter- aemia at Gregorio Marañ ́o ́n Hospital, Madrid, Spain. C. albicans germ tube antibody (CAGTA), mannan antigens (MN), antimannan antibodies (AMN) and (1→3)-b-D-glucan (BDG) were assayed using the manufacturer's and alternative cut-offs to improve the accuracy of the tests. The sensitivity of the biomarkers when used alone was low (58%284%), but specificity was high (65.8%292.0%). The best combinations were CAGTA and BDG using cut-offs of 1/80 and 80 pg/mL, respectively (sensitivity 96.8% and specificity 84%), and CAGTA and MN using cut-offs of 1/80 and 75 pg/mL, respectively (sensitivity 93.5% and specificity 86.0%). The sensitivity of both combinations was 100% for C. albicans, C. tropicalis and C. parapsilosis, but only combinations including BDG detected Candida krusei. The negative pre- dictive values (NPVs) of both combinations were, respectively, 97.7% and 95.6% (prevalence of candidaemia, 23.6%). For a prevalence of candidaemia of 5% and 10%, the NPV reached 99.8% and 99.6%. The combinations of CAGTA and BDG or CAGTA and MN had a very high NPV at the alternative cut-offs and could be used in antifungal stewardship programmes as a decision-making tool for discontinuing unnecessary empirical therapy in patients with suspected candidaemia.
He et al	2015	Serological response and diagnostic value of recombinant candida cell wall protein enolase, phosphoglycerate kinase, and β-glucosidase	Frontiers in Microbiology
		There are no specific signs and symtoms for invasive candidiasis (IC), which makes its diagnosis a challenge. Efforts have been made for decades to establish serological assays for rapid diagnosis of IC, but none of them have found widespread clinical use. Using a systemic candiasis murine model, serological response to recombinant proteins of enolase (rEno1), phosphoglycerate kinase (rPgk1), and β-glucosidase (rBgl2) were evaluated and rEno1 was found to possess the strongest immunoreactivity, followed by rPgk1 and rBgl2. Likewise, IgG antibody titers to rEno1, rPgk1, and rBgl2 in the positive sera of proven IC patients were determined by ELISA. Results show anti-rEno1 antibody possesses the highest titer, followed by rPgk1 and rBgl2. Antibodies against rEno1, rPgk1, and rBgl2 were detected by ELISA tests in a group of 52 proven IC patients or 50 healthy subjects, The sensitivity, specificity, positive and negative predictive values were 88.5, 90.0, 90.2, and 88.2% for anti-rEno1 detection, 86.5, 92.0, 91.8, and 86.8% for anti-rPgk1 detection, and 80.8, 90.0, 89.4, and 81.8% for anti-rBgl2 detection, respectively. The data clearly demonstrate that the recombinant proteins of Eno1, Pgk1, and Bgl2 are promising candidates for IC serodiagnosis. There's great possibility that the recombinant Eno1 will be more applicable in serodiagnosis and vaccine research on account of its strong serological response.
Leon et al	2012	Value of beta-D-glucan and Candida albicans germ tube antibody for discriminating between Candida colonization and invasive candidiasis in patients with severe abdominal conditions	Intensive Care Med
		Prospective study of 176 non-neutropenic patients, with SAC at ICU admission, and expected to stay at least 7 days. Surveillance cultures and BDG, CAGTA, CRP, and PCT levels were performed on the third day of ICU stay and twice a week for four consecutive weeks. Patients were grouped into invasive candidiasis (IC), Candida colonization, and nei- ther colonized/nor infected. The classification and regression tree (CART) analysis was used to predict IC in colonized patients. The dis- criminatory ability of the obtained prediction rule was assessed by the area under the ROC curve (AUC). The probabilities of IC were 59.3 % for the terminal node of BDG greater than 259 pg/mL and 30.8 % for BDG less than 259 pg/mL and CAGTA positivity, whereas there was a 93.9 % probability in predict- ing the absence of IC for BDG less than 259 pg/mL and negative CAG- TA. Using a cutoff of 30 % for IC probability, the prediction rule showed 90.3 % sensitivity, 54.8 % specificity, 42.4 % positive predictive value, and 93.9 % negative predictive value with an AUC of 0.78 (95 % confidence interval 0.76–0.81). Significant differences in CRP (p = 0.411) and PCT (p = 0.179) among the studied groups were not found. BDG with a positive test for CAGTA accurately differentiated Candida colonization from IC in patients with SAC, whereas CRP and PCT did not.
He et al	2016	Development of a Lateral Flow Immunoassay for the Rapid Diagnosis of Invasive Candidiasis	Frontiers in Microbiology

		Early and accurate diagnosis of invasive candidiasis (IC) is very important. In this study, a lateral flow immunoassay (LFIA) was developed to detect antibody against Candida albicans enolase (Eno). Colloidal gold particle labeled mouse anti human IgG (1.0 mg/L) was used as the detector reagent. Recombinant enolase (rEno, 1.0 mg/L) and goat anti IgG (1.0 mg/L) were immobilized in test and control lines, respectively, of a nitrocellulose membrane, acting as the capture reagents. The LFIA was used to detect anti Eno in 38 sera from clinically proven IC patients, as well as in 50 healthy control subjects. Compared with an indirect ELISA designed as a reference test, the specificity and sensitivity of the LFIA were 98.2 and 84.8%, respectively. Excellent agreement between the results obtained by ELISA and the LFIA (κ = 0.851) was observed in this study. In addition, the agreement between the blood culture results and LFIA test is strong (κ = 0.658). The data presented in the study indicate that the LFIA test is a suitable tool for the serological surveillance of IC in the field or in poorly equipped laboratories.	
Li et al	2013	Diagnostic value of immunoglobulin G antibodies against Candida enolase and fructose-bisphosphate aldolase for candidemia	BMC Infectious Diseases
		The yeast Candida is one of the most frequent pathogens isolated from bloodstream infections and is associated with significant morbidity and mortality. Problems with clinical and microbiological diagnosis of invasive candidiasis (IC) have prompted the development of non-culture-based laboratory methods. Previous reports suggest that serological detection of antibodies might be useful for diagnosing systemic candidiasis. Diagnosis of IC using antibodies against recombinant Candida albicans enolase (Eno) and fructose-bisphosphate aldolase (Fba1) was evaluated. Using recombinant Eno and Fba1 as coating antigens, enzyme-linked immunosorbent assays (ELISAs) were used to analyze sera from patients with candidemia (n = 101), Candida colonization (n = 50), bacteremia (n = 84), invasive aspergillosis (n = 40); and from healthy controls (n = 200). The results demonstrated that ELISA detection of anti-Eno and anti-Fba1 IgG distinguished IC from other pathogenic infections in patients and healthy individuals. The sensitivity, specificity, and positive and negative predictive values were 72.3%, 94.7%, 78.5% and 93% for anti-Eno, and 87.1%, 92.8%, 76.5% and 96.4% for anti-Fba1 antibodies, respectively. Combining these two tests improved sensitivity up to 90.1% and negative predictive value up to 97.1%, with specificity and positive predictive values of 90.6% and 72.2%. The tests were specific to the Candida genus and antibody titers were higher for candidemia patients than for controls. Positive antibody tests were obtained before blood culture results for 42.2% of patients for anti-Eno and 51.1% for anti-Fba1. These data suggest that tests that detect IgG antibodies against Candida enolase and fructose-bisphosphate aldolase, especially when used in combination, could be a powerful tool for diagnosing IC.	