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## **MEDICAL VERSUS SURGICAL THERAPY FOR CANDIDA ENDOCARDITIS: REVIEW OF 879 CASES AND A METAANALYSIS OF THE LITERATURE**

Steinbach WJ, Perfect JR, Benjamin Jr DK, Duke University, Durham, United States

**Background:** The current standard of care for *Candida* endocarditis includes surgery. The mortality of *Candida* endocarditis with medical therapy alone is thought to be higher than that achievable with adjunctive surgery. There are well-defined clinically-tested algorithms for medical and surgical therapy in bacterial endocarditis, but clinicians lack prospective clinical trial data for *Candida* endocarditis. We sought to review published treatment regimens of *Candida* endocarditis, including animal models, clinical reports, and observational series.

**Methods:** We conducted a MEDLINE search (1966 – December 2002) for all English language peer-reviewed articles related to *Candida* endocarditis. Inclusion criteria for the clinical case review required definite *Candida* endocarditis cases diagnosed by modified Duke criteria. We excluded cases where no antifungal therapy was employed, or there was not sufficient detail to determine antifungal therapy used or patient outcome.

**Results:** We reviewed a total of 879 *Candida* endocarditis cases from 418 reports. We analyzed a total of 163 cases of *Candida* endocarditis from 105 reports that met inclusion criteria. We also reviewed 13 animal model reports with 42 experimental antifungal treatment regimens. From these clinical reports, we were also able to evaluate 22 observational case-series for the treatment of *Candida* endocarditis using meta-analytic techniques. Amongst the 22 observational series, 97 patients were included. Reported mortality ranged from 0-100%, and there was evidence of heterogeneity (Egger  $p$ -value < 0.10). The most common medical therapy used was amphotericin B deoxycholate, and the most common combination regimen was amphotericin B deoxycholate + 5-fluorocytosine. We employed meta-regression using mortality as the outcome, and found that in studies where patients underwent adjunctive surgery for *Candida* endocarditis, there was a lower reported proportion of deaths [prevalence odds ratio (POR) = 0.56; 95% confidence interval (CI) = 0.16, 1.99]. Studies published prior to 1980 were associated with a higher reported mortality (POR = 2.03; 95% CI = 0.55, 7.61). Furthermore, in those studies where all of the patients received antifungal monotherapy there was a higher reported proportion of deaths (POR = 1.49; 95% CI = 0.39, 5.81). Similarly, studies where all of the patients were infected with *Candida parapsilosis* (POR = 1.51; 95% CI = 0.41, 5.52) or had left-sided *Candida* endocarditis (POR = 2.36; 95% CI = 0.55, 10.07) were also associated with a higher proportion of deaths.

**Conclusions:** Optimal antifungal therapy for *Candida* endocarditis is unknown. In our review of the medical literature there was substantial heterogeneity. There was a higher reported mortality in case series published prior to 1980 and in case series that reported exclusive use of antifungal monotherapy (generally amphotericin B deoxycholate). There was also a higher mortality rate in case series that reported a lower proportion of patients who underwent adjunctive surgery, infected with *C. parapsilosis*, or had left-sided endocarditis. With the recent availability of several new antifungals, including the echinocandins and other fungicidal therapies, management for *Candida* endocarditis should be revisited. We now have an appreciation for *Candida* endocarditis patients with poor outcomes and specific criteria for surgery should be integrated into future clinical study designs.