Positive peritoneal fluid fungal cultures in postoperative peritonitis after bariatric surgery

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Abstract

Postoperative peritonitis (POP) is a common surgical complication after bariatric surgery (BS). We assessed the importance of positive fungal cultures in these cases of POP admitted to the intensive care unit. Clinical features and outcome were compared in 25 (41%) *Candida*-positive patients (6 (22%) fluconazole-resistant *Candida glabrata*) and 36 patients without *Candida* infection. *Candida* infections were more commonly isolated in late-onset peritonitis and were often associated with multidrug-resistant bacteria. Risk factors for intensive care unit mortality (19.6%) were diabetes and superobesity. *Candida* infections, including fluconazole-resistant strains, are common in POP after BS. These data encourage the empirical use of a broad-spectrum antifungal agent. Clinical Microbiology and Infection © 2015 European Society of Clinical Microbiology and Infectious Diseases. Published by Elsevier Ltd. All rights reserved.

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Bariatric surgery (BS) is commonly performed for the treatment of morbid obesity [1]. Anastomotic leaks are one of the most frequent postoperative surgical complications, leading to admission to the intensive care unit [2]. These patients combine many conventional risk factors for fungal infection, such as prior surgery, broad-spectrum antibiotic use and severity of illness [3]. To assess the characteristics of fungal infections during postoperative peritonitis (POP) after BS, we compared the clinical features of patients with *Candida*-positive samples with those without *Candida*.

Between 1997 and 2012, all consecutive patients with a diagnosis of POP were prospectively analysed. Our microbiologic procedures have been previously described [4]. The mycology department performed fungus identification and susceptibility testing. According to European Committee on Antimicrobial Susceptibility Testing guidelines, *Candida glabrata* strains were considered to be not susceptible to fluconazole (http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/AFST/Antifungal_breakpoints_v_7.0.pdf).

Empirical antibiotic therapy, initiated at the time of reoperation, combined piperacillin/tazobactam or imipenem with amikacin and vancomycin possibly associated with antifungal therapy on the basis of presumed risk factors [5,6].

Demographic data, underlying diseases and clinical and surgical characteristics were collected at admission to the intensive care unit. Severity on the day of reoperation was assessed using the Acute Physiology and Chronic Health Evaluation II score [7]. The risk of fungal infection was assessed by the peritonitis score [6]. Therapeutic features and prognosis were recorded.

Results are expressed as mean (standard deviation) or numbers (proportions). *Candida*-positive and -negative patients were compared by the Student *t* and chi-square tests or by the Fisher exact test when required. Risk factors for death were assessed by univariate analysis followed by multivariate logistic regression analysis. Odds ratios and 95% confidence intervals were calculated. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and overall accuracy (OA) were calculated for the diagnostic tests. A value of $p < 0.05$ was considered significant.

Sixty-one patients were analysed (Table 1). A total of 27 fungi were cultured from peritoneal fluid in 25 (41%) patients (2 (8%) patients had fungaemia). Direct fungal examination of peritoneal fluid had a sensitivity of 20%, a specificity of 100%, a PPV of 100%, a NPV of 64% and an OA of 69%. Fungi were more frequently cultured from late-onset peritonitis (>day 15) (44% vs. 37.5% in early reoperation, p 0.03) and were associated with multidrug-resistant bacteria (Table 1). Susceptibility testing was available for 22 organisms, revealing six (27%)

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TABLE 1. Clinical and microbiologic characteristics and outcome of 61 patients admitted for postoperative peritonitis with or without fungal peritonitis

Characteristic	Total (n = 61)	Positive fungal culture (n = 25)	Negative fungal culture (n = 36)	p
Age (years), mean (SD)	43 (12)	44 (12)	43 (11)	0.67
Female gender, *n* (%)	43 (70)	18 (72)	25 (69)	0.83
BMI (kg/m^2), mean (SD)	48 (11)	49 (12)	48 (10)	0.71
Superobese, *n* (%)	15 (16)	7 (28)	8 (22)	0.61
Diabetes, *n* (%)	23 (38)	9 (36)	14 (38)	1
Initial surgery				
Sleeve gastrectomy, *n* (%)	14 (23)	7 (28)	7 (19)	0.54
Gastric bypass, *n* (%)	32 (52)	13 (52)	19 (53)	1
Reoperation before ICU admission, *n* (%)	26 (43)	10 (40)	16 (46)	0.79
Antibiotics before ICU, *n* (%)	33 (54)	16 (64)	17 (46)	0.20
Interval between initial surgery and diagnosis of POP, mean (SD)	14 (14)	17 (16)	12 (13)	0.27
Cause of postoperative peritonitis				
Gastrointestinal perforation, *n* (%)	25 (41)	9 (36)	16 (46)	
Anastomotic leak, *n* (%)	38 (62)	12 (48)	16 (46)	0.69
Abscess, *n* (%)	12 (20)	5 (20)	7 (20)	
APACHE II score, mean (SD)	18 (6)	20 (7)	17 (8)	0.08
Total no. of cultured bacteria	140	49	91	
Monomicrobial samples, *n* (%)	8 (13)	3 (12)	5 (14)	0.83
Multidrug-resistant bacteria, *n* (%)	14 (10)	9 (18)	5 (5)	0.03
No. of fungi	27	27	—	—
Candida albicans, *n* (%)	15	15 (56)	—	—
Candida glabrata, *n* (%)	6	6 (22)	—	—
Candida tropicalis, *n* (%)	2	2 (7)	—	—
Candida lusitaniae, *n* (%)	1	1 (4)	—	—
Outcome				
Duration of mechanical ventilation in survivors (days), mean (SD)		15 (12)	12 (12)	0.5
Length of ICU stay in survivors (days), mean (SD)		21 (14)	21 (19)	0.95
Mortality, *n* (%)		7 (28)	5 (14)	0.20

APACHE, Acute Physiology and Chronic Health Evaluation; BMI, body mass index; ICU, intensive care unit; POP, postoperative peritonitis; SOFA, Sequential Organ Failure Assessment.

fluconazole-resistant *C. glabrata*. The extraperitoneal fungal colonisation rate was 5% for the overall cohort and 4% in *Candida*-positive patients. No risk factors for fungal peritonitis were identified (Table 1). A grade C level of the peritonitis score (three or more risk factors) had 80% sensitivity, 72% NPV, 36% specificity, 42% PPV and 54% OA. Forty-one patients (67%) received empirical antifungal therapy (fluconazole n = 31, caspofungin n = 10), including 21 (58%) of 36 *Candida*-negative patients. All patients with a positive direct examination for fungi received empirical antifungal therapy. Four *Candida*-positive patients (16%) received inadequate therapy (fluconazole against *C. glabrata*). Empirical antifungal therapy remained unchanged in 13 cases (de-escalation in 3 cases and escalation in 3 cases). The mean duration of antifungal therapy was 18 ± 4 days (range 10–24 days). The mortality and morbidity rates were not different between the two groups (Table 1). Risk factors of death in univariate analysis are presented in Table 2. In multivariate analysis, diabetes (odds ratio 4.53, 95% confidence interval 1.03–17.64, p 0.044) and superobese patients (body mass index >50 kg/m^2) (odds ratio 4.38, 95% confidence interval 1.08–17.8, p 0.039) were significant risk factors for mortality.

A high rate of *Candida*-positive peritoneal fluid cultures and high rates of fluconazole-resistant strains were observed in this typical population of complicated BS patients. The presence of fungi in surgical samples was difficult to predict. Mortality and morbidity rates were similar in both groups. The presence of fungi in peritoneal fluid is not surprising in patients with prolonged infections [8]. However, our fungal culture rates appeared to be higher than those reported in several studies of

TABLE 2. Risk factors for mortality on univariate analysis

Characteristic	Dead (n = 12)	Survivors (n = 49)	p
Women, *n* (%)	7 (58)	36 (73)	0.31
Age, years, mean (SD)	47 (12)	42 (12)	0.22
BMI (kg/m^2)	54 (10)	46 (11)	0.04
Superobese, *n* (%)	6 (50)	9 (18)	0.022
Hypertension, *n* (%)	8 (67)	18 (37)	0.06
Diabetes, *n* (%)	8 (67)	15 (31)	0.02
Sleep apnoea syndrome, *n* (%)	4 (33)	10 (20)	0.35
Bypass, *n* (%)	7 (58)	25 (51)	0.66
Early intra-abdominal infection, *n* (%)	10 (83)	42 (86)	0.84
Antibiotics before ICU, *n* (%)	7 (58)	26 (53)	0.75
APACHE II score, mean (SD)	25 (7)	16 (7)	0.0003
SOFA score, mean (SD)	11 (4)	6.7 (3)	0.0009
Vasoactive agents, *n* (%)	10 (83)	31 (63)	0.19
Positive blood culture, *n* (%)	2 (17)	9 (18)	0.89
Peritoneal microorganisms, mean (SD)	2.1 (1)	2.7 (1)	0.08
Presence of Gram-negative bacilli, *n* (%)	6 (50)	33 (67)	0.27
Presence of Gram-positive cocci, *n* (%)	9 (75)	40 (82)	0.61
Presence of fungi, *n* (%)	7 (58)	18 (37)	0.18
Fungi reported on direct examination, *n* (%)	1 (8)	5 (10)	0.78
Adequate empirical antibiotic therapy, *n* (%)	10 (83)	36 (73)	0.70
Adequate empirical antifungal therapy, *n* (%)	11 (92)	42 (86)	0.59

APACHE, Acute Physiology and Chronic Health Evaluation; BMI, body mass index; ICU, intensive care unit; SOFA, Sequential Organ Failure Assessment.

POP [9–11]. Only two studies in complicated BS have reported the presence of *Candida* in 31% to 37% of cases [4,12]. Postoperative changes in host microbiota could be proposed as a driving force for the emergence of *Candida,* as fungal colonization has been reported in the excluded and functional parts of the stomach of patients who have previously undergone gastric bypass surgery [13]. The clinical relevance of positive fungal samples in surgical patients remains a subject of debate. Untreated *Candida* colonization is usually rapidly cleared from the peritoneal space. In some cases, true infection occurs, with intra-abdominal abscesses, persistent growth on repeated surgeries and a risk of dissemination [14]. The progressive colonization of extraperitoneal sites can only be documented by repeated cultures [15]. However, the vast majority of these patients are referred from surgical wards without surveillance programmes. Our data demonstrated the poor predictive value of clinical criteria. The peritonitis score has a very low PPV, which could be explained by the over-representation of two criteria in our population (70% of women and 100% of upper gastrointestinal surgery). Fungal biomarkers such as β–D-glucan could be of interest to identify those patients who really need to be treated [16]. Several articles suggest a link between fungal cultures and poorer outcome [9,10,17], especially with gastroduodenal perforations [9,17]. The high rate of fluconazole-resistant strains previously reported [18] supports the empirical use of echinocandins due to the potential risk of increased mortality in the case of delayed therapy [19]. However, no clinical study has ever assessed the need to treat *Candida* peritonitis. Our cohort is obviously underpowered to draw any conclusions on mortality issues (258 patients would be necessary to conclude on the role of *Candida*). Several limitations of our study have to be stressed. This single-centre survey performed in a reference centre may not provide a reliable picture of complicated BS cases. The global prevalence of fungi in these patients might be underestimated, as our analysis was limited to the first reoperation.

In summary, *Candida* strains are frequently cultured from surgical samples in POP after BS. The high rates of fluconazole-resistant strains and the failure to identify any risk factors for positive fungal samples justify providing empirical broad-spectrum antifungal treatment.

Transparency declaration

All authors report no conflicts of interest relevant to this article.

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