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Early postoperative candida colonization in alimentary canal in patients undergoing open heart surgery

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Aim. **To examine the frequency and factors predisposing to candidiasis in the digestive tract in the early postoperative period after open heart surgery.**

Methods. **One hundred patients undergoing open heart surgery were enrolled in this study. Patients were divided into 2 groups in regard to *Candida* spp. colonization. Group A means increased *Candida* spp. colonization after open heart surgery (31/100). Group B indicates unchanged *Candida* spp. colonization after open heart surgery (69/100). Samples were obtained from both oral and anal mucosa in 3 different periods of operation: 1) preoperatively (stage 1), 2) at the end of the first hour in the intensive care unit (stage 2), 3) 24 hours after operation (stage 3). Findings were compared with both preoperative and intraoperative parameters. For fungal isolation Sabourauds dextrose agar and blood agar were used.**

Results. **In Group A (31), there was a significant relationship between the samples in stage 1 and 2 ($p=0.031$), and also a significance between stage 1 and 3 ($p=0.048$). Comparison between *Candida* positive and negative groups (Group A and B) did not reflect any statistical significance ($p>0.05$).**

Conclusion. ***Candida*** **colonization in the alimentary canal in the early postoperative period after open heart surgery is due to individual preoperative features. However, early postoperative *Candida* colonization in the digestive tract is not a risk factor for sepsis unless the patient has an additional risk factor leading to prolongation of length of stay in the intensive care unit.**

Key words: ***Candida*** **colonization - Mycosis - *Candida albicans* - Candidiasis - Open heart surgery - Cardiopulmonary bypass - Intensive care unit.**

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Nosocomial candidemia has increased during the past 2 decades and now accounts for 10% to 20% of all nosocomial bloodstream infections. Reports of this serious infection estimated with case-fatality rates of 20% for children and 50% for adults pointed out that The National Nosocomial Infections Surveillance System reported that the *Candida* species has become the fourth most common nosocomial blood culture isolate in the United States.[1, 2]

According to previous literature, 17% of all intensive care unit patients developed deep fungal infections, particularly due to the *Candida* species.[3] On the other hand, the incidence of *Candida* infections (*e.g.* sepsis, mediastinitis) after open heart surgeries were reported in different ratios like 20.3%[3] or 7.5%.[4]

Studies also proved the significance of the resistance of the host patient to opportunistic infections. The resistance of the host patient is markedly reduced in critically ill people.[5] To prevent postoperative nosocomial infections like candidemia, many preoperative methods like selective decontamination of the digestive tract were described for severely diseased patients undergoing surgery.[6]

Based on the above reports, the goals of this prospective study were: 1) to determine preoperative and intraoperative risk factors for early postop-

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TABLE I.—*Types of the operations.*

	N. (%)
CABG	78 (78)
CABG+MVR	8 (8)
CABG+AVR	4 (4)
MVR	4 (4)
ASD	3 (3)
AVR+MVR	2 (2)
AVR	1 (1)

CABG: coronary artery bypass grafting; MVR: mitral valve replacement; AVR: aortic valve replacement; ASD: atrial septal defect.

erative *Candida* colonization in the digestive tract after cardiopulmonary bypass (CPB) and 2) to list the long-term results of this early colonization.

Material and methods

Patients

One hundred patients undergoing open heart surgery were enrolled in this study. The types of open heart surgeries are summarized in Table I.

Patients were divided into 2 groups with regard to *Candida* spp. colonization. Group A means increased *Candida* spp. colonization after open heart surgery (31/100). Group B indicates unchanged *Candida* spp. colonization after open heart surgery (69/100).

This prospective study was approved by the Ethics Committee of Inonu University. Besides, each participant in the study was included after his/her confirmation in writing.

Exclusion criteria

Those patients who had had any symptomatic fungal or other infection, patients who had had any previous fungal infection in the last 3 months, patients who had used any antibiotic therapy in the last 3 months, patients who had been admitted to hospital with any disease in the last 3 months, patients who had had any additional immunosuppressive disease, patients who were being treated with immunosuppressive drug therapy, patients who were not willing to participate in the study were not included.

Sampling

Samples were obtained from both oral and anal mucosa in 3 different periods of operation: 1) preoperatively (stage1); 2) at the end of the first hour in the intensive care unit (stage 2); 3) after 24 hours of operation (stage 3).

The samples were collected with sterilized swabs and immediately placed in Stuart's transport media.

D-Yeast; isolation and identification

Swabs were plated onto Sabouraud's dextrose agar (Becton Dickinson, France) supplemented with 50 mg/L chloramphenicol and blood agar. After incubation at 30 °C for 48 hours, colony counts were performed visually. Identification was based on production of germ tubes and observation chlamydospores on cornmeal agar.

Follow-up

All patients were treated with the same group of antibiotics (cefazolin sodium+amikacin) for their prophylaxis. After 3 days of operation, the antibiotic regime was stopped.

According to the literature, if an infection occurs up to 3 days after hospital discharge or within 30 days of an operative procedure, it's attributed to the admitting hospital, ward, or surgical procedure.[7] That's why each patient included in the study was followed up in regard to any infective symptoms both in the period of hospitalization after surgery and also after discharge.

Statistical analysis

Findings were compared with both preoperative and intraoperative parameters. Statistical calculations were performed on the SPSS V 8.0 computer program by statisticians. Independent Sample T test, Paired Samples T test, Oneway Anova test, Wilcoxon Signed Ranks Test, Mann Whitney U test were used. Data was considered to be significant when p value was less than 0.05.

Results

Descriptive findings of patients and comparisons were summarized in Table II.

The patients (100) were divided into 2 groups: Group A (31) and Group B (69). All microbiological evaluations indicated only one type of pathogens: *Candida* spp.

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TABLE II.—*Descriptive findings in each group are seen. In addition, comparisons between the groups were listed with their p values. Please note that there is not any significant difference between Group A and B in regard to any parameter.*

	Group A	Group B	p
Age (mean)	57.42	57.35	0.97*
Weight (mean)	67.39	69.94	0.33*
Length (mean)	163.19	165.06	0.37*
Smoking (packet/year)	13.22	22.4	0.06*
WBC (mean)	8.44	7.86	0.35*
Eosinophil (mean)	2.10	2.23	0.77*
Sedimantation (mean)	25.74	25.66	0.98*
Cholesterol (mean)	189.23	199.07	0.51*
CPB (min) (mean)	103.58	107.28	0.67*
Cross clamp (min) (mean)	77.53	80.59	0.82*
AAD (n)	4	2	0.58*
DM (n)	8	10	1*
CTI	55	54	0.28**
Pulmonary edema (n)	8	7	1*
Sex			
Male (n)	20	46	0.83*
Female (n)	11	23	

WBC: white blood cell; CPB: cardiopulmonary bypass; AAD: associated atherosclerotic disease; DM: diabetes mellitus; CTI: Cardiothoracic Index. *) One way Anova. Post Hoc test. **) Mann-Whitney U test.

In Group A (increased *Candida* spp. colonies, 31 patients), there was a significant relationship between stage 1 and 2 (p=0.031), and also a significance between stage 1 and 3 (p=0.048). However, there was no significance between stage 2 and 3 (p=0.346).

In regard to mean levels of numbers of colonies in Group A, there was a 17.61-fold increase between stage 1 and 3.

When comparing the groups to each other, no comparisons showed statistical significance (p>0.05). According to these comparisons, increased *Candida* spp. colonization after CPB (Group A), did not have any inferior feature than the group with unchanged *Candida* spp. colonization after CPB (Group B). In regard to CPB time or aortic x-clamp time, there was no statistical difference between Group A and Group B (p>0.05) (Table II).

The groups were compared to each other according to sex and age of the patients (Table III). There was no statistical difference. Besides, different age groups in Group A were compared to each other to understand whether a specific age group is prone to postoperative candidiasis or not. However, in Group A, no specific age group prone to candidiasis was obtained. None of the patients exhibited any problem after their discharge.

TABLE III.—*Comparisons between the groups in regard to both age groups and sex. There is no any statistically significant difference between the groups in regard to age groups and sex (p> 0.05).*

Age groups	Group A (31)	Group B (69)
Female		
<30	1	1
31-50	1	2
>50	9	20
Male		
<30	1	0
31-50	5	14
>50	14	32

Discussion

Although only few reports indicating the aggressiveness of *Candida* spp. after cardiac surgery [8] can be found in the literature, the incidence of invasive fungal infections in a certain group of patients treated with total parenteral nutrition or prolonged broad-spectrum antibiotics has considerably increased.[3] Mediastinitis after aorto-coronary bypass surgery due to *Candida albicans* was reported with a ratio of 7.5%,[4] however it was pointed out [7] that a mortality rate attributable to candidemia of 50% was observed. Michalopoulos *et al.* reported that the mortality rate in cardiac surgery patients with systemic candidemia was 27.2%, whereas it was only 1.5% in patients without candidemia.[3] According to different reports, nosocomial candidemia has increased during the past two decades and now accounts for 10% to 20% of all nosocomial bloodstream infections. Reports on this serious infection estimated to have fatality rates of 20% for children and 50% for adults pointed out that The National Nosocomial Infections Surveillance System reported that the *Candida* species has become the fourth most common nosocomial blood culture isolate in the United States.[1, 2] In a review by Eggimann *et al.*,[7] severity score of disease, shock on admission, prolonged length of Intensive Care Unit (ICU) stay, age >60 years, size of the unit (>10 beds), parenteral nutrition, antimicrobial therapy, central venous access, days with arterial line, mechanical ventilation, tracheostomy, device utilization ratio, neurologic failure at day 3, intracranial pressure monitor were all described as overall risk factors for nosocomial infections in ICU. *Candida* infections are a group of noso-

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comial infections, and despite the decreased ratio of *Candida* infection, some subgroups of fluconazole-resistant *Candida* infections tend to increase.[7]

Because of the facts listed above, we aimed to determine the predictors of *Candida* colonization after open heart surgery. As seen in the literature, studies on candidemia particularly include patients stayed in ICU for prolonged durations.[1-3, 7, 9] We questioned whether CPB is a reason for postoperative candidemia, or if prolonged CPB is just a result like postoperative opportunistic infections. Or with another expression, is it true that prolonged CPB and postoperative infections are the results of preoperative patient factors? We thought that previous papers in the literature were related to the late postoperative period. Whereas, if it's true as has been written in previous reports, that prolonged CPB is a predictor of postoperative candidiasis, then we should find a relationship between CPB and early postoperative *Candida* spp. colonization. So, we planned to evaluate the early postoperative period for previous reports proving that many contributory factors due to CPB might predispose to the spread of *Candida* into the circulation due to translocation from gut into blood.[10, 11] This might be important for detecting in the early postoperative period since it has been reported that *Candida albicans* commonly colonizes mucocutaneous areas of the body in immunosuppressed patients, a disease process readily treated by use of topical and/or oral absorbable or nonabsorbable antifungal agents.[12] That's why we decided to evaluate *Candida* colonization in the alimentary canal and mucosal samplings of two different ends of the digestive tract, both oral and anal mucosa, were used for measurement purposes.

We didn't see any significant effect of CPB on *Candida* colonization. However, when comparing stage 1 to 3 in the increased *Candida* spp. colonization group (Group A) mean levels of *Candida* colonization have a 17.61-fold increase. These results reflect that open heart surgery is not a direct cause of *Candida* colonization since there is no statistical difference between the comparison of Group A and Group B. Nevertheless, CPB serves as a contributory factor because of the increase of colonies seen in Group A. This conclusion implies that CPB is not a reason for *Candida* spp. colonization because CPB times do not reflect a difference between Group A and B (Table II). Consequently, we think that even prolonged CPB is not a cause for systemic candidiasis, CPB and prolonged CPB is a result like postoperative opportunistic infections. They are all the result of poor preoperative conditions. If a patient is severely diseased and is in poor condition preoperatively, he/she will encounter many complications in both the intraoperative and postoperative period. These complications include prolongation of CPB and ICU stay, and also colonization of opportunistic pathogens. The main factor is the patient's individual features, like resistance to infections. Others like CPB are not direct causes. Maybe the term "contributory factor" is more suitable to describe their roles. A review of previous literature, evidences reports that support our findings.

For example, after reviewing their 2 512 consecutive patients who had undergone aorto-coronary bypass surgery, Antunes *et al.* found mediastinis in 60 patients. Cultures were positive in 40 of 60 patients, and *Candida albicans* occurred in 3 of 40 patients (7.5%). However, according to their report, they couldn't find any relationship between mediastinitis and age, sex, smoking, hypertension, family history of coronary artery disease, history of myocardial infarction, emergency/urgent operation, high angina class, number of diseased vessels, left main disease, left ventricular dysfunction, CPB time, postoperative respiratory failure, reoperation for bleeding, perioperative myocardial infarction or postoperative stroke.[4] In another report, Michalopoulos *et al.*[3] concluded that a significant percentage of patients who remained in an ICU for more then 9 days developed systemic candidiasis. They noticed that the risk factors for systemic candidiasis are prolonged mechanical ventilation, prolonged ICU stay, development of postoperative infection and consequent administration of antibiotics, presence of central venous catheters, patient ages, history of diabetes mellitus and administration of total parenteral nutrition. They found that the patients who developed systemic candidiasis had prolonged bypass time and aortic cross clamp time and all received inotropic agents and total parenteral nutrition. As seen in their findings, cardiopulmonary bypass time is not a direct relating factor. The main risk factor is the reason for open heart surgery. Besides, the patient's condition in both preoperative and postoperative stages due to his/her main disease is also a predictor for systemic candidiasis. If the patient is in poor condition, that will result in a prolonged ICU stay and consequent candidiasis. Otherwise, the inner dynamics of CPB do not appear to be responsible. According

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to our results, open heart surgery increases *Candida* spp. colonization, however we couldn't find any difference in CPB times between Group A and Group B. Consequently, it's possible to say that open heart surgeries are risk factors for more *Candida* spp. colonizations, but not direct reasons for systemic candidiasis. Individual patient factors are the most important factors for postoperative candidiasis.

In a report on prolonged candidemia after congenital heart surgery, Chakrabarti *et al.* found the duration of total parenteral nutrition (TPN) and documentation of a thrombus in a central vessel to be the most important risk factors for candidemia. Receiving multiple courses of antibiotics, TPN, central venous catheters, abdominal surgery, extensive burns, corticosteroid usage were determined as other factors.[1] As reviewed in another report by Michalopulos,[2] diabetes mellitus, antibiotics, staying in an ICU more then 8 days, mechanical ventilation for more than 9 days, central venous or Swan-Ganz catheters, were determined as risk factors for candidemia by previous studies. In their study, they observed that diabetes mellitus, duration of CPB (>120 min), aortic cross clamp time (>70 min), red blood cell transfusion, low cardiac output syndrome, use of ≥2 inotropes for 24 hours, intra-aortic pump, acute renal failure, re-exploration, use of central venous catheter >72 hours, TPN, bacteremia/bacterial infection, use of ≥2 antibiotics for >72 hours, length of ICU stay ≥9 days, ongoing mechanical ventilation ≥10 days were significantly associated with candidemia. As pointed out by Michalopoulos *et al.*, prolonged conventional CPB is a risk factor for increased postoperative transfusion requirements and frequency of re-exploration, postoperative renal dysfunction, and increased length of ICU stay. Prolonged CPB is also associated with increased aortic cross clamp time, increased risk for postoperative low cardiac output syndrome and ischemia-related gastrointestinal dysfunction. Gastro-intestinal dysfunction sets the prolonged total parenteral nutrition. As seen in the algorithm above, all the factors leading to candidemia are a result of prolonged CPB.

However, as we mentioned above, this algorithm does not start with prolonged CPB. Prolonged CPB is not a cause. It's a result like the others. It's link in the chain. The main reason is the patient in poor condition. Poor condition due to the severity of disease in a patient prolong the duration of CPB. Consequently, predictors for postoperative candidemia should be sought from the preoperative stage. Factors like prolonged CPB should be considered as contributory factors. We believe that the examination of patient's preoperative individual feature is the most important factor for predicting postoperative candidemia.

According to the guidelines for the prevention of surgical site infection,[5] the increased proportion of surgical site infection caused by *Candida* spp. is believed to be due to increasing numbers of severely ill surgical patients and the impact of widespread use of broad-spectrum antimicrobial agents. The risk of surgical site infection can be conceptualized by this equation:

$$\frac{\text{dose of bacterial contamination} \times \text{virulence}}{\text{resistance of host patient}} = \text{risk of surgical site infection}$$

As seen in this equation, the resistance of the host patient is one of the major factors in the risk of surgical site infection. Besides, it's obvious that the patient's individual features at the preoperative stage are responsible for patient resistance . The main reason is the severity of the illness, which reduces the resistance of the patient. Others are contributory effects. In a normal range of CPB duration, *Candida* spp. colonization after surgery is not dependent on CPB. As seen in our results, there was no difference in regard to CPB time between the increased *Candida* spp. colonization after CPB (Group A) and unchanged numbers of *Candida* spp. after CPB (Group B). Despite similar CPB time, some patients had increased *Candida* spp. colonization, but the rest of them did not. Likewise, Gardlund determined that the length of operation, time on cardiopulmonary bypass, age, diabetes, type of operation or the time span from operation until sign of infection was not associated with a special bacterial etiology.[13]

Conclusions

In conclusion, CPB should be described as a contributory factor. The main reason is the host patient's resistance. Goals should be directed at decreasing the effect of contributory factors to prevent postoperative candidemia. One of the important factors is antibiotic usage after surgery. Prolonged antibiotic prophylaxis seems to provide no benefit in decreasing wound infections and might increase the risk of

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acquired antibiotic resistance.[14-16] The reason why we didn't see any symptom relating to candidemia in our patients, may be that the antibiotic regime in our protocol was interrupted at 72 hours. Although reports revealed that problems due to *Candida* colonization can easily be solved by fluconazole treatment,[17] we didn't have any problem with our patients with *Candida* spp. colonization in their digestive tract, so no one needed any antifungal therapy.

Another method to prevent candidiasis may be selective decontamination of the digestive tract, which can be performed in the preoperative stage of severely diseased patients.[6,18] However, use of this method should be restricted to high-risk cardiac patients. This is because, based on our results, early postoperative *Candida* spp. colonization in the alimentary canal does not lead to candidemia in a patient unless his/her preoperative condition is poor. Early mobilization in the ICU and early hygienic oral care and shortening of ICU stay are enough to prevent the conversion of mucosal colonization into candidemia. A supporting report has revealed that standard hygienic protocols can reduce the rates of *Candida* infections.[7]

Finally, CPB is a contributory factor for postoperative candidiasis. The main reason is the host patient's resistance. Early postoperative *Candida* spp. colonization in the digestive tract will not lead to candidemia if the patient is mobilized early and prophylactic antibiotic usage is shortened.

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