

Peer Review File

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Reviewer A

Thank you very much for the opportunity to review this study. This study is a retrospective data about HSV and CMV esophagitis in five centers. After excluding HIV infection, both immunocompetent and immunocompromised had chance of VE infection. The detail of patients characteristic and other factors were well described. My comments are as below;

Line 128 how GERD was diagnosed (by MII-pH, histopathology, symptom or EGD finding)

Line 139 and method how did the authors choose participants into the control groups?

Method - please add the exclusion criteria ex. HIV-patients

Table 2 and 3 the number of CMV and HSV esophagitis are not equal to N=50.

Comment 1: Line 128 how GERD was diagnosed (by MII-pH, histopathology, symptom or EGD finding).

Reply 1: We did not review how patients were diagnosed with GERD. Patients with GERD were identified based on past medical history/ICD code on chart review.

Changes in the text: No changes in the text.

Comment 2: Line 139 and method how did the authors choose participants into the control groups?

Reply 2: Unmatched random sampling of controls with ratio of 1:5 to increase study power to detect meaningful differences.

Changes in the text: This study included 246 randomly sampled control group with 1:5 ratio.

Comment 3: Method - please add the exclusion criteria ex. HIV-patients

Reply 3: patients with a diagnosis of HIV/AIDS were excluded, and patients younger than 18.

Changes in the text: This retrospective case-control study identified patients older than 18 years old and diagnosed with either HSV or CMV esophagitis by histopathologic examination or by confirmatory immunohistochemical staining. Cases were obtained through a free text search using pathology reports from MedStar Health Hospitals, which includes five hospitals across the District of Columbia and Maryland between 2009-2022. Patients with a diagnosis of HIV/AIDS or younger than 18 were excluded from the study.

Comment 4: Table 2 and 3 the number of CMV and HSV esophagitis are not equal to N=50.

Reply 4: The summation of CMV and HSV is 49 given that one case was a coinfection with CMV and HSV as indicated in line 53.

Changes in the text: None.

Reviewer B

1. Figure 1: Please provide the full name of "VE" in Figure 1 legend.

2. Tables:

1) Please provide the header of the first column in all tables.

	Immunocompetent N=17	Immunocompromised N=33	P-value
Gender			0.740

2) Please indicate how data is presented for Age and BMI in Table 1, 3-4.

Age (years)	57 (18.9)	63 (15.9)	0.021*
Race			0.169
White	20(40%)	126 (51.2%)	
Black	25(50%)	109 (44.3%)	
Asian	2(4%)	2 (0.8%)	
Others	3(6%)	9 (3.7%)	
BMI (kg/m2)	26.27 (9.21)	27.73 (7.47)	0.298

3) Should the below percentage be “52%”? 17/33=?

149 were on immunosuppressive therapy, 17 (51%) were on systemic steroids, eight (24%) had DM, five
 150 (15%) had undergone organ transplant, five (15%) had ESRD and were on dialysis. Additionally, thirteen
 151 (39%) had an active malignancy, with colon cancer being the most common, followed by esophageal,
 152 breast, and multiple myeloma. Refer to **Table 1** for a summary of patients' demographic comorbidities.

4) Please check the percentages in Table 1, 3-4.

Heavy alcohol use	5 (11.6%) (missing = 7)	42(17%)	0.372
Tobacco use	12 (27.3%) (missing = 6)	122 (49.6%)	<0.01*

5) Please provide the full name of “EGD” in Table 2, “CMV”, “HSV” in Table 3.

Reply: Thank you for your comments. We have revised the text accordingly.