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The treatment outcome of CMV infection in critically ill patients who have received gastrointestinal surgery

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Introduction

1. There are different studies discussing cytomegalovirus (CMV) infection in immunocompromised patients. Ganciclovir, Valganciclovir, cidofovir, etc., were the treatment options for these patients. Generally speaking, CMV infection is usually self-limited in immunocompetent patients; therefore, these antiviral medications' efficacy and side effects were not well-established. However, the risk of CMV infection or reactivation in critically ill immunocompetent patients was higher than previously thought. We are interested in the treatment outcome of this group of people. The duration of the treatment is also a topic to be discussed.
2. We collected the clinical data from Taichung Veterans General Hospital (VGHTC) database and analyzed the factors affecting survival in CMV-infected critically ill immunocompetent patients. We would like to know whether infected end-organ removal can affect survival. Because some organs can be safely removed in a range without catastrophic consequences, therefore we chose gastrointestinal surgery patients to analyze for the effect of end-organ resection.

Method

1. This retrospective study collected clinical data from the database of VGHTC between March/2012 and May/2022. It aimed to find out the treatment outcome of CMV-infected patients in intensive-care unit who have received gastrointestinal operations. 575 critically ill patients were diagnosed with CMV, among them, 66 gastrointestinal surgery patients fit the inclusion and exclusion criteria of our study.
2. The inclusion criteria of this study are 1. CMV positive (i.e. CMV QPCR positive, CMV DNA positive, or CMV positive in pathologic specimen) and 2. ever admitted to intensive-care unit during the course of gastrointestinal surgery hospitalization. The exclusion criteria included 1. patient age under 18 years old or 2. ever received organ transplantation surgery or 3. under long-term immunosuppressive and immunomodulator medication. Association factors of survival were analyzed. The primary outcome is the survival of the ganciclovir administration duration.
3. Data in the study were analyzed by IBM SPSS version 22.0 (International Business Machines Corp, New York, USA). Cox proportional hazard model was used to assess survival time and several covariant factors including age, sex, initial APACHE II score at intensive-care-unit admission, duration of ganciclovir use, number of co-morbidities, and CMV infected end-organ resected by operation.

Discussion

1. CMV infections in immunocompetent patients are usually self-limited, so it is a challenge to evaluate the treatment outcome from a prospective study. It is difficult to assess whether the recovery from the infection is due to the patient's immune system or the benefit of the antivirals. There is no consensus on CMV treatment in immunocompetent patients. This retrospective study revealed a positive trend in the efficacy of ganciclovir for more than 14 days in critically ill immunocompetent CMV-infected patients. Fig.1 and Table 2
2. The ganciclovir uses for more than 14 days has a better survival outcome compared to less than 14 days(HR: 0.259, 95% CI(0.101, 0.662), *p* value=0.005). Increasing the number of co-morbidities also leads to a higher mortality rate(HR:1.37; 95%CI:1.143, 1.642; *p* value=0.0006.) Table 2
Age, sex, APACHE II score, and resection of CMV-infected organs have no significant impact on survival.

Conclusion

Although the resection of CMV-infected organs has no impact on survival benefits. Using ganciclovir for more than 14 days has a positive survival outcome on critically ill immunocompetent patients, but more co-morbidities imply poor survival. The weak point of this study is that the sample size is small, and further studies should be made for more patient numbers.

Result

Table 1: Patient characteristics

Characteristics	Patients(n=66)	
Age(year)	71.55±13.09	
Body mass index	23.45±3.78	
Sex	Female	Male
	22(33.3%)	44(66.7%)
APACHE II score	26.35±7.19	
Co-morbidities, n(%)	yes	no
Hypertension	38(57.6%)	28(42.4%)
Diabetes mellitus	21(31.8%)	45(68.2%)
Ischemic heart disease	21(31.8%)	45(68.2%)
Cerebrovascular disease	14(21.2%)	52(78.8%)
Hyperlipidemia	19(28.8%)	47(71.2%)
Chronic obstructive pulmonary disease	13(19.7%)	53(80.3%)
Peripheral vascular disease	8(12.1%)	58(87.9%)
Chronic kidney disease	24(36.4%)	42(63.6%)
Number of co-morbidities, n(%)		
0	16(24.2%)	
1	12(18.2%)	
2	13(19.7%)	
3	6(9.1%)	
4	5(7.6%)	
5	6(9.1%)	
6	5(7.6%)	
7	2(3.0%)	
8	1(1.5%)	
Survival status on discharge after the GI surgery	Alive	Dead
	41(62.1%)	25(37.9%)
Duration of hospitalization (day)	61.36±36.10	
Duration of intensive care unit stay (day)	34.62±30.02	
Ganciclovir administration	≧14day	<14day
	35(53%)	31(47%)
CMV detection by operation specimen	yes	no
	42(63.6%)	24(36.4%)
CMV detection site	yes	no
Blood	40(60.6%)	26(39.4%)
Gastrointestine	48(72.7%)	18(27.3%)
Bronchoalveolar lavage	8(12.1%)	58(87.9%)
GI Operation site		
Upper GI	6(9.1%)	
Lower GI	46(69.7%)	
Abdomen or both upper and lower GI	14(21.2%)	
Duration of long-term follow up(month)	16.58±23.52	

-Age, body mass index, APACHE II score, duration of hospitalization, duration of intensive-care-unit stay, duration of long-term follow up revealed by mean with standard deviation

--Data showed the number of patients and percentage was shown in parenthesis

Table2: Cox regression analysis of survival on discharge after the gastrointestinal surgery

	Univariate			Multivariate		
	HR	95% CI	*p* value	HR	% CI	*p* value
Age	1.04	1.004, 1.077	0.031*	1.029	0.989, 1.069	0.157
Ganciclovir use						
<14 d	Ref.			Ref.		
≧14d	0.369	0.159, 0.856	0.02*	0.259	0.101, 0.662	0.005*
APACHE II score	1.047	0.993, 1.103	0.086	0.983	0.916, 1.056	0.645
CMV-infected end-organ resected by operation						
yes	Ref.			Ref.		
No	1.309	0.591, 2.900	0.508	1.802	0.760, 4.272	0.181
Sex						
Female	Ref.			Ref.		
Male	1.255	0.522, 3.020	0.612	0.786	0.306, 2.031	0.623
Number of co-morbidities	1.352	1.166, 1.568	0.000*	1.370	1.143, 1.642	0.0006*

-HR: Hazard ratio; 95% CI: 95% confidence interval; CMV: cytomegalovirus; APACHE II score: Acute Physiology and Chronic Health Evaluation II score

*p<0.05

Figure 1: Kaplan-Meier survival curve

