

## **Response to Reviewer's Comments and Suggestions**

ESPS No. 23794: Video Capsule Endoscopy in Left Ventricular Assist Device

Recipients with Obscure Gastrointestinal Bleeding

We are very grateful for reviewers' thoughtful comments and suggestions. As outlined below, we have fully addressed and clarified all the issues raised point-by-point. We have also revised our manuscript accordingly.

### **Reviewer 00058448**

Minor comments

1. Results, the authors "Among patients with positive VCE, the recurrent bleeding rate did not differ whether subsequent endoscopy was performed". It is interesting to know after VCE, whether the clinical management of patients change? i.e. drug dose adjustment ?

#### **Response:**

After VCE, medications were adjusted in 7 out of 12 patients with positive VCE, and 8 out of 18 patients with negative VCE. These changes included discontinuation or decrease in the dose of aspirin, and initiation of proton pump inhibitors. The change of medical management did not affect the rate of recurrent bleeding regardless of whether patients had a positive VCE (40% vs 57.1%,  $p = 1.00$ ), or negative VCE (60% vs 50%,  $p = 1.00$ ). The above findings are now included in the manuscript on page 12, the last paragraph.

2. Discussion, "Using logistic regression, we found that higher INR on presentation was associated with a higher probability of positive findings in VCE". The result of logistic regression was not shown in the table.

#### **Response**

The result of logistic regression is described in the Results section on the manuscript page 11-12: "Using logistic regression, we found that higher INR on presentation was

associated with a higher probability of positive findings in VCE (OR = 3.62. 95% C.I. = 1.03-12.7,  $p = 0.04$ ), adjusted for age, gender, and hemoglobin level”.

3. Conclusion, "An observation-and-supportive care approach could be an alternative way to treat LVAD patients with OGIB." Before this conclusion, do all patient with OGIB and LVAD receive VCE in the hospital ? or is there any selection bias for VCE for these patients ?

#### Response

All patients were treated and all procedures (including VCE) were performed as inpatients, as mentioned in the first paragraph of the Result section on manuscript page 10, and Material and Methods in the section of Procedures on page 7. Therefore, we do not think that there is a selection bias.

#### **Reviewer 01438558**

The authors presented a retrospective study as the title “Video capsule endoscopy in left ventricular assist device recipients with obscure gastrointestinal bleeding. This experience is interesting. However, there are a few comments with the current study that need to be addressed. My comments are as follows: Major comments

1. Did the authors do special managements for patients during capsule endoscopy (e.g. Holter electrocardiography)?

#### Response

Upon admission, all LVAD patients were monitored by continuous telemetry and evaluated serially by staff. LVADs were monitored continuously by the system controller and interrogated immediately after the VCE via the system monitor to evaluate for any changes in function. We have clarified this in the Material and Methods section in the paragraph under Procedures, on manuscript page 8.

2. Were there any small intestinal lesions treated by balloon or spiral endoscopy in this study? If so, the authors should mention some comments and prognosis after the procedure.

#### Response

Three patients were treated by single-balloon enteroscopy. This is described in the last paragraph of the Result section on page 12, and Table 3 (patient No. 8, 10, and 11). As listed in Table 3, patient No.8 and No. 10 developed recurrent hematochezia and anemia requiring further endoscopic treatment, whereas patient No. 11 had no further bleeding.

3. Are there any differences of small intestinal lesions between the patients with LVADs and those without LVADs of advanced heart failure?

Response

This is an interesting question. This study investigated obscure GI bleeding in LVAD patients, and did not include advanced heart failure patients without LVAD; therefore we were not able to distinguish the differences of small intestinal lesions between heart failure patients with or without LVAD based on this study. In fact, after extensive literature search, to our knowledge no study has ever been done to directly answer this question.

However, in our current study of LVAD patients, 1/3 were found to have small intestinal angiodysplasias, and half of the patients were found to have small intestinal bleeding without lesions identified, presumably due to angiodysplasia given that it has been shown to be the most common cause of GI bleeding in LVAD patients (Table 2, and page 14 in the Discussion). It is well known that heart failure is strongly associated with small intestinal angiodysplasias with an OR of 4.22 (*Scan J Gastroenterol* 2013; 48(4):433-8). It is also known that angiodysplasia is the most common cause of small intestinal bleeding (*Am J Gastroenterol* 2015; 110:1265-1287). Therefore, angiodysplasia likely is the leading cause of small intestinal lesion in heart failure patients without LVAD, just like patients with LVAD.