ORIGINAL

Postoperative hemodynamic changes for predicting anastomotic leakage after esophagectomy in patients with esophageal cancer using the FloTrac system

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Abstract : Background : Anastomotic leakage after esophagectomy is significantly associated with more severe complications, such as sepsis and mortality. Early prediction for anastomotic leakage is usually difficult and needs to be treated rapidly. In the current study, we investigated the correlation between hemodynamic and several complications after esophagectomy in patients with esophageal cancer, using the FloTrac system. Materials and Methods : Between April 2013 and December 2014, 39 patients with a mean age of 66.6 ± 8.9 years underwent postoperative supervision using the FloTrac sensor/Vigileo monitoring system after curative surgery for esophageal cancer. We retrospectively evaluated the association between the number of aberrant cardiac index (CI) along with stroke volume variability (SVV) values and clinicopathological parameters of postoperative complications in this report. Results : There were significant positive correlations between the number of aberrant values of CI along with SVV and depth of invasion during pathological stage. Concerning major postoperative complications, there was a significant positive correlation between the number of aberrant values of CI and anastomotic leakage. Discussion: The hemodynamic change by employing the FloTrac system could predicts the complication of anastomotic leakage after esophagectomy. Adequate management of hemodynamic stability by utilizing it will reduce the complications of anastomotic leakage. J. Med. Invest. 67 : 240-245, August, 2020

Keywords **:** *Prediction of anastomotic leakage, Esophageal cancer, FloTrac system*

INTRODUCTION

Esophageal cancer is among the leading causes of cancer-related deaths worldwide and is often characterized by lymph node (LN) metastases throughout the cervical, mediastinal, and abdominal regions. Despite recent improvements in surgical techniques and adjuvant therapies, prognosis in patients with advanced disease has not developed adequately (1, 2). Moreover, perioperative management of esophagectomy is very important. Significant caution and preservation of operation is necessary because complications of esophagectomy may sometimes cause death, depending on circumstances. A lot of reports have showed the artifices to prevent postoperative complications. The causes of anastomotic leak can be multi-factorial ; however, major contributing factors include surgical technique and inadequacy of blood supply (3, 4), coupled with patient-related variables such as malnutrition, smoking as well as use of non-steroidal anti-inflammatories drugs.

Anegg *et al*. reported supply of oxygen at the anastomosis of the gastric conduit reaches higher levels after orthotopic than retrosternal gastric transposition (5). Therefore, the pressure of manubrium was suggested to be the main reason for hypoxia. Kunisaki *et al*. reported that partial resection of the manubrium could significantly reduce the incidence of leak in the retrosternal procedure (6). Campbell *et al*. reported that conduit vascular evaluation is associated with reduction in anastomotic leak after esophagectomy (7). Moreover, Wiggins T. *et al*. reported omentoplasty could be employed as an adjunct technique to reduce the incidence of anastomotic leak in esophageal anastomosis (8). However, they also reported that these results were not observed in colorectal anastomosis (8). Anastomosis leakage has been a persistent complication of esophagectomy regardless of technical improvement. Therefore, early recognition along with treatment of anastomotic leak are crucial because they have been associated with increased patient mortality in esophageal cancer.

The FloTrac sensor in combination with the Vigileo monitor (Edwards Lifescience, Tokyo, Japan) is a less invasive hemodynamic monitoring device than those used for thermodilution assessment ; furthermore, it can be used to continuously monitor cardiac output (CO), as well as stroke volume, and stroke volume variation (SVV) through a peripheral arterial pressure line. Moreover, the non-invasive FloTrac sensor does not require calibrated CO monitoring. The advantage of this option is that highly valuable information can easily be obtained by the system, which is directly connected to the arterial pressure waveform. We previously reported surgical procedures that affect the hemodynamics using the FloTrac system in patients with esophageal cancer following esophagectomy (9). As a result, we demonstrated that the retrosternal route potentially influences the haemodynamic stability measured by the FloTrac/Vigileo system (9). Besides the consideration of previous study, we newly investigated the correlation between hemodynamic and several complications after esophagectomy in patients with esophageal cancer, using the FloTrac system. Postoperative prediction of complications using FloTrac system after esophagectomy may become mainstream in the near future.

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MATERIALS AND METHODS

Patient characteristics

Between April 2013 and December 2014, 39 patients (31 males, eight females) with a mean age of 66.6 ± 8.9 (range, 45–81) years underwent postoperative monitoring by the FloTrac sensor/Vigileo monitoring system after esophagectomy for esophageal cancer at Gunma University Hospital. Resectability was determined by conventional staging methods (computed tomography (CT), ^{18}F-flourodeoxyglucose position emission tomography (^{18}F-FDG-PET), endoscopic ultrasonography as well as esophagography).

Monitoring by the FloTrac sensor/Vigileo monitoring system was performed in the intensive care unit (ICU). Each patient gave written informed consent before esophagectomy. Preoperative examinations regarding operable tolerance included heart, respiratory, renal, and hepatic functions, and all enrolled patients passed the preoperative examinations. Preoperative echocardiographic measurements of the left ventricular ejection fraction were normal in all patients. Patients with pacemakers, a history of cardiac arrhythmia, severe peripheral vascular disease along with patients who had cardiac support, persisting mitral, or aortic dysfunction after surgery were excluded (9). Furthermore, patients with preoperative treatment also were omitted.

Patient characteristics are shown in Table 1. Tumor stage and disease grade were assigned according to Guidelines for the clinical and pathological studies on carcinoma of the esophagus (10th edition) (10). Intramural metastasis of stomach was recognized in pStage4b case. As a result, two pT4 cases were included in this study. One case was diagnosed as R2 operation because metastatic LN invaded to left subclavian artery. Operation procedure and complications of this study are shown in Table 2.

The mean operative time in the 39 patients in the esophagectomy population were 531.3 ± 79.6 minutes. A total of 26 (66.6%) patients underwent radical surgery for esophageal cancer performed using a right thoracoabdominal approach in the current study. Remnant 13 (33.3%) patients underwent surgery using the thoracoscopic approach. 31 (79.5%) patients underwent esophagectomy with an extended three-field lymphadenectomy, and the remaining eight patients (20.5%) underwent two-field lymphadenectomy. The overall morbidity rate including surgical and nonsurgical complications in the esophagectomy population was 41.0% (16/39). Anastomotic leakage (20.5%) and pulmonary complications, including pneumonia (15.4%) and heart complication (5.1%) were recognized among the postoperative management (Table 1). There was no reoperation case after esophagectomy.

Table 1. Patient characteristics (n=39)

Sex	M 31 : F 8
Age (years; mean ± SD)	66.6 ± 8.9
Depth of invasion (pT)	
0 / 1 / 2 / 3 / 4	1 / 19 / 2 / 15 / 2
Lymph node metastasis (pN)	
0 / 1 / 2 / 3 / 4	14 / 10 / 7 / 6 / 2
Stage (pStage)	
0 / 1 / 2 / 3 / 4a / 4b	5 / 5 / 13 / 12 / 3 / 1

Table 2. Operation procedure and complications (n=39)

Esophagectomy	
thoracoscopic surgery	13
traditional surgery	26
Reconstruction Route	
postmediastional route	35
retrostinal route	3
antethoracic route	1
Fields of lymphadenectomy	
2 fields	8
3 fields	31
Operation time (minutes; mean ± SD)	531.3 ± 79.6
Postoperative complication	16 (41.0%)
heart complication	2 (5.1%)
pulmonary complication	6 (15.4%)
anastomotic leakage	8 (20.5%)
ICU stay (hours; mean ± SD)	35.2 ± 13.4

Postoperative care and assessment of hemodynamic parameters in ICU

Postoperative care and assessment of hemodynamic parameters in ICU were drawn in previous report (9). The FloTrac/Vigileo system monitors (Edwards Lifescience, Irvine, CA, USA) CO, CI, stroke volume (SV), stroke volume index, and SVV. We retrospectively calculated and analyzed CI and SVV values in ICU. CI is indicated as CO (L/min)/patient body surface. SVV (%) similarly equals (maximum SV-minimum SV)/mean SV, where maximum and minimum SV are the mean values of the four extreme values of SV during a period of 30s, and the mean SV is the average value for this period of time.

Postoperatively, all patients were kept intubated and ventilated overnight in ICU, and if their clinical condition was satisfactory, they could extubated next morning. The 21-bedded ICU was available to all patients with esophageal cancer and staffed by anesthetists and experienced nurses. Data of FloTrac sensor were collected from the patients admitted to ICU, and the length of their stay was recorded. CI and SVV were evaluated by recording the number of aberrant values. Numbers of aberrant CI and SVV were counted from the ICU record, although total numbers of measurement differed in each case because total lengths of ICU stay were different. In this study, CI values < 2.2 and SVV values > 10 were considered aberrant as previous reports. A cutoff value of CI was based on the Forrester subset, and the cutoff value of SVV was defined as 10 because the normal range of SVV was 10 to 15. CI and SVV observations are recorded as numerical values measured at regular intervals every hour. The vertical axis of the figures is the average of the number of abnormal values in each comparative group, and the CI is a small number as the average value since the CI often changes within a substantially normal range. Since the abnormal value of SVV reflects a decrease in the amount of circulating blood, it is a large number because the number frequently changes in the postoperative period. Based on the above criteria, we retrospectively evaluated the association between the number of aberrant

CI as well as SVV values and clinicopathological parameters of postoperative complications in this report.

STATISTICAL ANALYSIS

The relationship between the number of aberrant CI along with SVV values and clinicopathological parameters of postoperative complications after esophagectomy were analyzed by ANOVA. Probability (*P*) values < 0.05 were considered to indicate statistically significant difference.

RESULTS

There were significant positive correlations among the number of aberrant values of CI as well as SVV and depth of invasion (p = 0.008 and p = 0.005, respectively), along with pathological stage (p = 0.019 and p = 0.026, respectively) (Figures 1 and 2). On the other hand, there were no significant correlations among the number of aberrant values of CI together with SVV and LN metastases of esophageal cancer (Figure 3). Concerning to major postoperative complications, there was a significant positive correlation between the number of aberrant values of CI and anastomotic leakage (Figure 4). Esophageal cancer patients with anastomotic leakage significantly showed aberrant value of CI during postoperative period. However, there were no significant correlations among the number of aberrant values of CI as well as SVV and pulmonary complications along with heart complication (Figures 5 and 6).

DISCUSSION

Hemodynamic stability management by utilizing the FloTrac/Vigileo system after esophagectomy is useful to safely perform postoperative management in patients with esophageal cancer. The FloTrac/Vigileo system device uses arterial pressure waveform analysis to calculate SV and CO. Furthermore, it does not require calibration against an independent CO measurement. Therefore, it provides a method to determine hemodynamics status, changes in the clinical course, and responses to therapeutic intervention in patients who have arterial catheters in place (11).

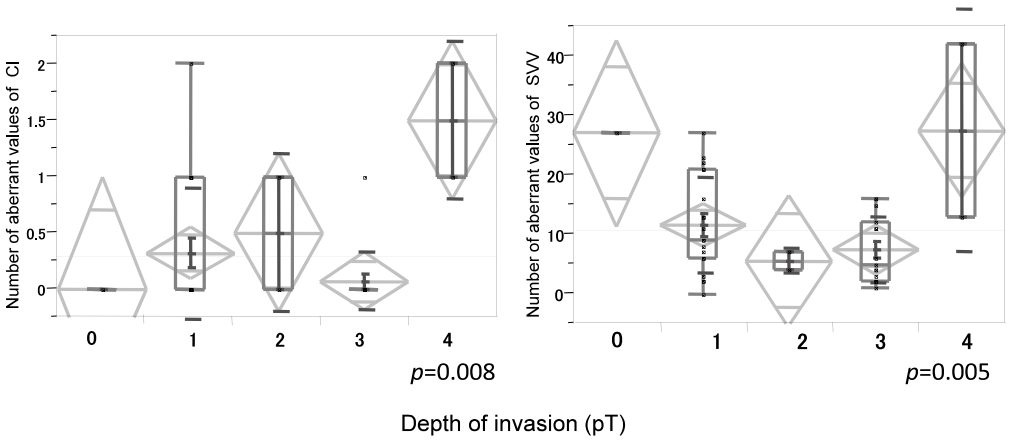

Figure 1. Correlations among the number of aberrant values of CI along with SVV and depth of invasion (pT)
There were significant positive correlations between the number of aberrant values of CI along with SVV and depth of invasion (p = 0.008 and p = 0.005, respectively).
※ The diamonds represent the sample mean and its confidence interval. The box plot shows a concise representation of the distribution of values, and blue line shows confidence interval and it's mean value.

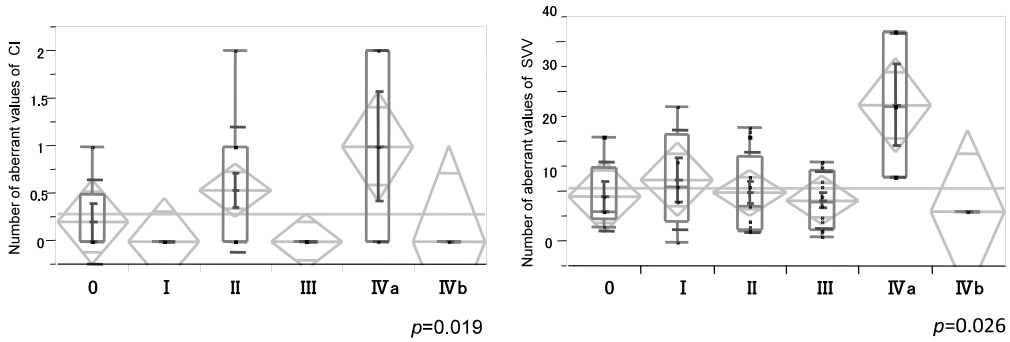

Figure 2. Correlations among the number of aberrant values of CI along with SVV and pathological stage (pS)
There were significant positive correlations among the number of aberrant values of CI along with SVV and pathological stage (p = 0.019 and p = 0.026, respectively).

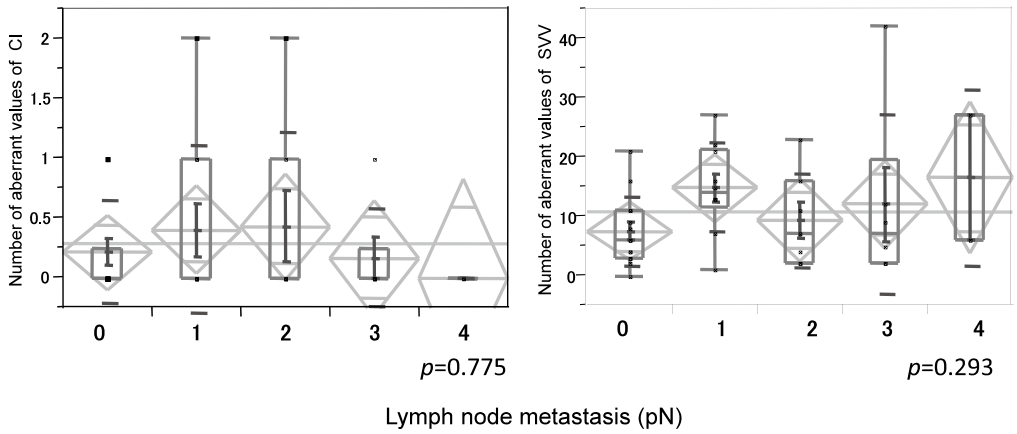

Figure 3. Correlations among the number of aberrant values of CI along with SVV and lymph node metastasis (pN)
There were no significant correlations among the number of aberrant values of CI along with SVV and lymph node metastasis of esophageal cancer.

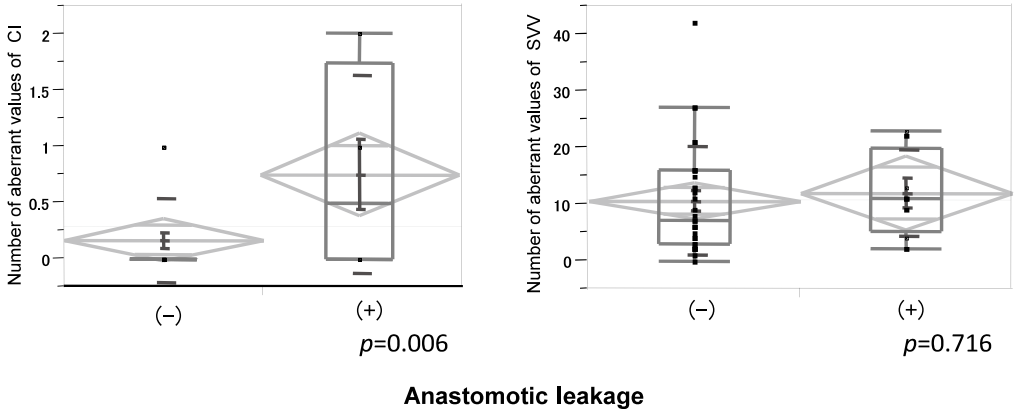

Figure 4. Correlations among the number of aberrant values of CI along with SVV and anastomotic leakage
There was a significant positive correlation between the number of aberrant values of CI and anastomotic leakage.

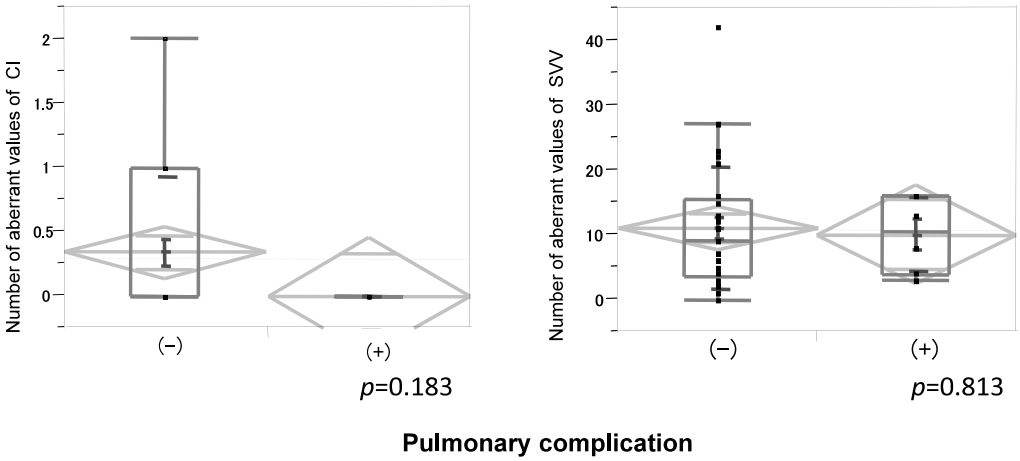

Figure 5. Correlations among the number of aberrant values of CI along with SVV and pulmonary complication
There were no significant correlations among the number of aberrant values of CI along with SVV and pulmonary complications.

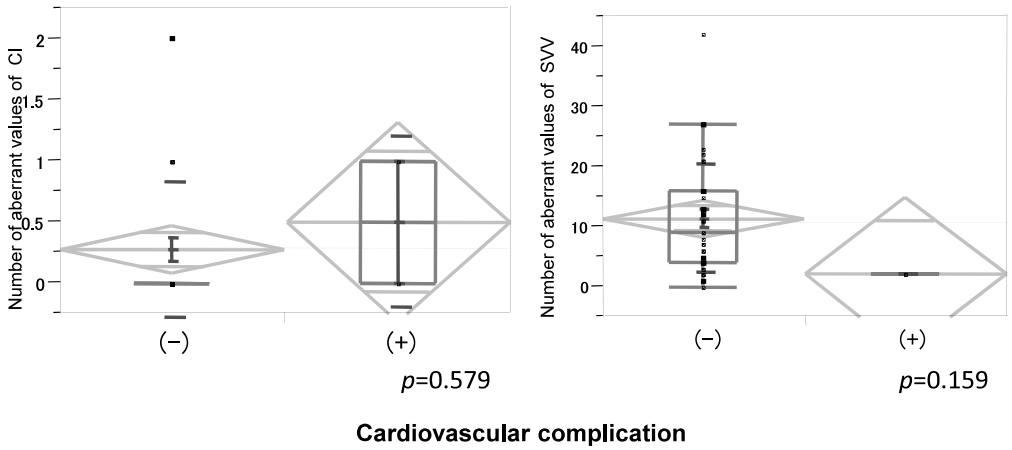

Figure 6. Correlations between the number of aberrant values of CI along with SVV and heart complication
There were no significant correlations among the number of aberrant values of CI along with SVV and heart complication.

We previously reported that surgical procedures could affect hemodynamics in esophageal cancer patients after esophagectomy, using the FloTrac system (9). In the current report, we also continuously studied association between the number of aberrant CI along with SVV values and clinicopathological parameters or following complications after esophagectomy. As a result, there were significant positive correlations between the number of aberrant values of CI as well as SVV and depth of invasion in pathological stage. As the depth of invasion of the tumor progresses, operation time and surgical invasion increase due to resection. Moreover, cases of the depth of invasion of the tumor progresses may have chronic dehydration than many shallow cases, because it is likely that the amount of dietary is low from before. On the other hand, SVV is changing rates of respiratory variation of stroke volume and it has been consistently shown to be reliable predictor of fluid responsiveness in adults. An increase in SVV indicates a decrease in circulating blood volume. Therefore, it is considered that CI and SVV significantly showed more aberrant values in cases of the depth of invasion of the tumor progresses compared with shallow cases in proportion to the depth of invasion. In addition, these results reflect that T4 cases of cancer which were judged during operation, retrosternal route significantly had been selected for getting surgery compared with other routes in this study. We previously reported the retrosternal route potentially influences the haemodynamic stability (CI or SVV) measured by the FloTrac/Vigileo system (9). We routinely select postmediastinal route in patients with esophageal cancer and R0 resection in recent year. However, retrosternal route was selected in a case where we evaluated the possibility of remnant cancer cells in the operation because progressive remnant cancer affects normal passage of reconstruction conduit in the future. Therefore, advanced esophageal cancers tend to be selected the reconstruction of retrosternal route.

Concerning major postoperative complications, the number of aberrant values of CI had significantly positive correlation with anastomotic leakage. Moreover, surgical treatment has an acceptable mortality in high volume centers, although high rates of postoperative morbidity have been described (12-15). However, pulmonary complications and anastomotic complications like leakage and stenosis are still common (13-15). Anastomotic leakage following esophagectomy is significantly associated with morbidity and mortality. A major factor determining anastomotic success is an adequate blood supply to the conduit. Postoperative variation of hemodynamic stability influences the stable supply of blood to the conduit. Anastomotic leakage may be caused by unstable blood supply of conduit.

Anastomotic leakage usually becomes apparent after measuring the CI or SVV during the ICU stay. As a result, our data may show the number of aberrant values of CI during ICU stay, which can predict the complication of anastomotic leakage after esophagectomy. Regarding to correlation between CI and anastomotic leakage, it is not clear whether it is the consequence or cause in examining the time course of appearance of aberrant CI and anastomotic leakage. Kusano C *et al*. reported oxygen delivery 6 h after esophagectomy correlates with anastomotic leakage and severe pneumonia and may be a determinant of hospital mortality (16). As one hypothesis, decreasing of CI in postoperative early phase will lead to appearance of anastomotic leakage because reduced oxygen delivery due to decreasing cardiac output correlates with anastomotic leakage. Although there is likely to be a correlation with SVV, it is considered that there was no difference because the total number of cases was small and infusions were given immediately as needed as an index of postoperative management from the result of value of SVV. Therefore, adequate management of hemodynamic stability by employing the FloTrac/Vigileo system after esophagectomy is important, and it will reduce the complications of anastomotic leakage. However, hemodynamic after esophagectomy was greatly influenced by several factors, regardless of our previous report which did not confirm the correlation between hemodynamic and perioperative balance intraoperative blood transfusion along with correlation between intraoperative bleeding and balance of intraoperative infusions (9).

Thus, our data by FloTrac/Vigileo system, which may show the number of aberrant values of CI during ICU stay, is one of the predictors of complication of anastomotic leakage. In current study, there were no significant correlations among the number of aberrant values of CI along with SVV and pulmonary complications as well as heart event. We think rapid and adequate drug intervention using blood gas analysis or monitoring of heart rate in ICU cannot cause aberrant data of hemodynamic. In summary, according to the present data, obtained by using the FloTrac system, demonstrated that locally advanced esophageal cancer

which needed reconstruction of retrosternal route significantly tends to show that the aberrant data of CI and postoperative hemodynamic change can predict anastomotic leakage after esophagectomy for esophageal cancer patients.

The limitation of this study is the small number of cases, thus it is necessary to accumulate data from further cases.

DISCLOSURE AND FUNDING STATEMENT

The authors have no financial conflicts of interest to disclose concerning the study.

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