

# 論文内容要旨

Prediction of anastomotic leakage after left-sided  
colorectal cancer surgery:  
a pilot study utilizing quantitative near-infrared  
spectroscopy

(左側大腸癌手術における縫合不全の予測：  
近赤外線分光法を用いたパイロット研究)

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**Background:**

Anastomotic leakage (AL) is one of the most serious complications in colorectal surgery. The reported incidence of colorectal anastomotic leakage is 3%–21%. It not only increases the emotional and physical burden on the patient, but also has a negative impact on prognosis. It is well known that many risk factors can cause the occurrence of postoperative anastomotic leaks, such as male sex, preoperative radiotherapy, and a low rectal anastomosis. Intestinal anastomotic blood flow is also considered an important factor in AL. However, a method for assessing the intestinal blood flow has not yet been established. Recently, the effectiveness of blood flow evaluation using indocyanine green (ICG) has been reported and verified in several clinical trials regarding the prevention of postoperative AL. However, this method of evaluation has limitations in terms of quantitation and objectivity and cannot be used for patients with drug allergies. Considering these limitations, we focused on the measurement of tissue oxygen saturation (rSO<sub>2</sub>) using an INVOS™ (manufactured by Covidien), a device that employs near-infrared spectroscopy (NIRS) to quantitatively measure oxygen saturation in tissues. We planned this study to examine whether tissue oxygen saturation measurement using INVOS™ is useful for assessing anastomotic intestinal blood flow and whether it contributes to the prevention of AL.

**Materials and methods:**

Patients Seventy-three patients with left-sided (from descending colon to rectum) colorectal cancer who underwent surgery at Hiroshima University Hospital from 2017 to 2019 were enrolled in this study. Consistent with the guidelines of the Declaration of Helsinki, this study was authorized in advance by the institutional review board of Hiroshima University Hospital(E2019-1742).

Outcomes Endpoints were correlation between rSO<sub>2</sub> and AL and analysis of risk factors including rSO<sub>2</sub> for AL.

Operations and measurement of rSO<sub>2</sub> Depending on the location of the tumor, left hemicolectomy, sigmoidectomy, high anterior resection, low anterior resection or very low anterior resection was selected. The surgical procedures are briefly described here. Conventional open surgery was performed in patients with bulky tumor or with a history of major abdominal surgery. Other patients underwent laparoscopic surgery via a medial-to-lateral approach. Vascular ligation with lymph node dissection was performed in the standard fashion. Preservation of the left colonic artery was left to the surgeon in charge. In this study, rSO<sub>2</sub> was performed using the INVOS 5000C oximeter (Medtronic, Minneapolis, MN). After mesenteric division, the rSO<sub>2</sub> value of the colon at the site of proximal transection (oral side of anastomosis) was measured. The measurement of rSO<sub>2</sub> was performed within 5 min after the mesenteric division, three times, and the median value was recorded. Reconstruction was performed using an end-to-end double stapling technique. A diverting stoma was installed at the operator's discretion. AL was diagnosed based on clinical symptoms and signs such as changes in drain coloration and the presence of fever with peritonitis. On radiographic examination, AL was diagnosed based on the presence of contrast leakage on digestive tract radiography, gas accumulation around the anastomosis site, and discontinuity of the intestinal wall on computed tomography.

Statistical analysis Mann–Whitney U test was used to compare variables between the AL patients

and No-AL patients. A multivariate logistic regression analysis was utilized to determine predictors of AL in the current cohort.

### **Results:**

rSO<sub>2</sub> was able to be measured successfully in all cases, and there were no adverse events related to the measurement of rSO<sub>2</sub> during surgery. The rSO<sub>2</sub> values ranged from 50% to 95% (median, 83%). The median rSO<sub>2</sub> value at the oral anastomotic site was 86.5% in sigmoidectomy, 79% in high anterior resection, 82% in low anterior resection and 72% in very low anterior resection. Although the rSO<sub>2</sub> value tended to be lower in very low anterior resection group than in the sigmoidectomy group, there was no statistically significant difference in rSO<sub>2</sub> measurements by anastomotic level. AL was found in 6 of 73 patients (8.2%), showing the patient characteristics and surgical parameters in AL and No-AL patients. AL more frequently occurred in male, but there were no significant differences in the body mass index (BMI), history of cardiovascular disease, pulmonary disease or diabetes or long-term use of steroids. Regarding the surgical parameters, significant differences were observed in the estimated blood loss, tumor site and rSO<sub>2</sub> of the proximal anastomotic site. In patients with AL, the estimated blood loss was greater (30 g vs. 87 g,  $p=0.03$ ) than in No-AL patients. AL occurred more frequently in patients with tumors located at the lower rectum than in others (17.2% vs. 2.3%,  $p=0.02$ ). The median rSO<sub>2</sub> value of the proximal anastomotic site in AL patients was significantly lower than that in non-AL patients (64.5% vs. 83.0%,  $p=0.01$ ). An ROC curve analysis revealed that the cut-off value of rSO<sub>2</sub> for predicting AL was 65.0%. In the multivariate analysis, a low rSO<sub>2</sub> value at the proximal anastomotic site was extracted as an independent risk factor associated with AL (odds ratio 30.0 [95% CI 1.97-1282.1]  $p=0.01$ ). Five of 6 patients with AL in the lower rectum were noted, so a subgroup analysis focusing on patients with lower rectal cancer was conducted. A low rSO<sub>2</sub> value and estimated blood loss were shown to be risk factors for AL in the univariate analysis, but only a low rSO<sub>2</sub> value was an independent risk factor for AL in the multivariate logistic regression analysis (odds ratio 21.9 [95% CI 3.12-154.1]  $p=0.02$ ).

### **Conclusion:**

In this pilot study, we examined the exploratory application of rSO<sub>2</sub> measurement using INVOS™ for the evaluation of intestinal tissue perfusion. The patients who experienced AL tended to have low rSO<sub>2</sub> values at the site of anastomosis; thus, the measurement of colonic rSO<sub>2</sub> may provide some information on the condition of the anastomotic site. However, since the study population was relatively small and the results were limited, it is necessary to confirm these results in a larger cohort. A prospective multicenter study (study number: UMIN000038179) is currently underway with a larger cohort to evaluate the utility of rSO<sub>2</sub> measurement as a clinical tool to assess bowel perfusion.