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# Postoperative delirium in liver resection patients: Usefulness of the abdominal wall fat index

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Postoperative delirium is one of the most common and important complications in patients who have undergone surgery. Although the precise mechanism of postoperative delirium is unclear, several risk factors have been reported. Here we investigated candidate risk factors for postoperative delirium after liver resection. This retrospective analysis included 112 consecutive patients who underwent an elective liver resection. Preoperative and intraoperative parameters were analyzed for their potential as risk factors of postoperative delirium. Thirty-one patients (27.7%) developed postoperative delirium. A multivariate analysis showed that advanced age (odds ratio [OR] = 1.189, 95% confidence interval [95%CI] = 1.081–1.309, p<0.001), the abdominal wall fat index (AFI) (OR 14.904, 95%CI 3.072–72.319, p<0.001), and non-laparoscopic surgery (OR 5.496, 95%CI 1.237–24.413, p=0.025) were independent risk factors for postoperative delirium. The AFI had a high OR for postoperative delirium. The area under the receiver-operating characteristic (ROC) curve was 0.806 (95%CI, 0.713–0.896) with a calculated optimal cut-off value of 1.0. The AFI is thus the most useful predictor for postoperative delirium after liver resection. Elderly patients with a higher AFI (>1.0) and open liver resection are associated with an increased risk of postoperative delirium.

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**Key words:** postoperative delirium, abdominal wall fat index, AFI, elderly, risk factor

## Introduction

Postoperative delirium is one of the most common and important complications in patients who have undergone surgery. Postoperative delirium is associated with prolonged hospital stay, higher morbidity and mortality rates, and increased costs (1–3). Although the precise mechanisms underlying postoperative delirium are unclear, several risk factors have been reported including advanced age, male sex, alcohol abuse, dementia, invasive procedure, disorders of metabolism, and atherosclerosis (4–7). Some reports stated that patients who underwent a liver resection showed a high risk of postoperative delirium (8, 9). However, reliable risk factors for developing postoperative delirium after liver resection are not yet clear.

The most common etiology for liver resection is hepatocellular carcinoma (HCC). Several reports demonstrated that the risk of developing HCC from chronic hepatitis due to the hepatitis B or C virus is known to be age-dependent, and the mean age of HCC patients has been getting higher (10, 11). The incidence rate of atherosclerosis has been rising with the rapid progression of aging in many societies (12). Several studies focused on the relationship between postoperative delirium and atherosclerosis (13–15). Kawamoto et al. (16) reported that the abdominal wall fat index (AFI) was a useful parameter for evaluating atherosclerosis. In this study, we investigated whether postoperative delirium was associated with several candidate risk factors, including the AFI.

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## Patients and Methods

### *Patients*

This retrospective analysis was undertaken in patients who underwent liver resection at the National Hospital Organization Nagasaki Medical Center between January 2016 and February 2018. During this period, 112 consecutive patients who underwent an elective liver resection were enrolled in this study. The following preoperative and intraoperative parameters were analyzed for their potential as risk factors of postoperative delirium: age, gender, body mass index (BMI), AFI, diagnosis, presence of liver cirrhosis, existence of anemia, diabetes mellitus, respiratory disorder, ischemic cerebrovascular disease, a history of alcohol abuse, operative time, intraoperative blood loss, and operative method.

The presence of postoperative delirium was assessed with the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV). We separated the patients into two groups: a postoperative non-delirium group, and a postoperative delirium group. Informed consent for their data to be used was obtained from all patients, and the study protocol was approved by the Ethics Committee of National Hospital Organization Nagasaki Medical Center (Certificate no. 30002).

### *Abdominal wall fat index (AFI)*

We measured the thickness of the preperitoneal and subcutaneous fat layer by computed tomography (CT). The maximal thickness of preperitoneal fat (Pmax) at the anterior surface of the liver and the minimal thickness of subcutaneous fat (Smin) in the upper median abdomen were measured. The abdominal wall fat index (AFI) was estimated by calculating the Pmax/Smin ratio (Fig. 1) (16).

### *Statistical analysis*

Numerical data were evaluated using the Mann-Whitney *U*-test for nonparametric data and the Chi-square test or the Fisher exact test for categorical data, are the results are presented as the median and range. The utility of the predictors was ascertained using sensitivity and specificity calculations and receiver-operating characteristic (ROC) analyses. The statistical analyses were carried out using SSPS ver. 23 software (SSPS, Chicago, IL). P-values <0.05 were considered significant.

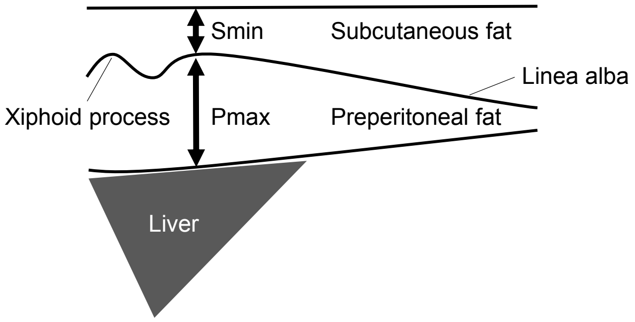

**Figure 1.** The maximal thickness of preperitoneal fat (Pmax) at the anterior surface of the liver and the minimal thickness of subcutaneous fat (Smin) in the upper median abdomen were measured by CT. The abdominal wall fat index (AFI) was estimated by calculating the Pmax/Smin ratio.

## Results

Among the 112 consecutive patients who underwent liver resection, 31 patients (27.7%) developed postoperative delirium. The perioperative clinical characteristics of the patients with and without postoperative delirium are summarized in Table 1. According to a univariate analysis, there were no significant differences between the non-delirium and delirium groups in gender, BMI, etiology for liver resection, presence of liver cirrhosis, ischemic cerebrovascular disease, operation time, intraoperative blood loss, or operative method. However, the patients' ages were significantly higher in the delirium group compared to the non-delirium group (median, 75 years vs. 67 years, respectively; p<0.001). The AFI values were also significantly higher in the delirium group compared to the non-delirium group (median, 1.3 vs. 0.8, respectively; p<0.001). The rates of the presence of anemia (35.5% vs. 14.8%), diabetes mellitus (41.9% vs. 21.0%), and respiratory disorder (41.9% vs. 21.0%) were significantly higher in the delirium group compared to the non-delirium group. The rate of a history of alcohol (48.8% vs. 21.0%) was significantly higher in the delirium group compared to the non-delirium group, as was the rate of non-laparoscopic surgery (84.0% vs. 63.0%, respectively).

According to the multivariate analysis, advanced age (odds ratio [OR] = 1.189, 95% confidence interval [95%CI] = 1.081–1.309, p<0.001), the AFI (OR 14.904, 95%CI 3.072–72.319, p<0.001), and non-laparoscopic surgery (OR 5.496, 95%CI 1.237–24.413, p=0.025) were significant independent risk factors for postoperative delirium (Table 2).

**Table 1.** Perioperative clinical characteristics of patients with or without postoperative delirium

| Characteristics | Non-delirium (n=81) | Delirium (n=31) | p-value |
|---|---|---|---|
| Age | 67 (32–83) | 75 (58–88) | <0.001 |
| Gender, male/female | 55/26 | 21/10 | 1.000 |
| BMI | 23.1 (16.8–32.0) | 21.6 (15.4–30.4) | 0.234 |
| AFI | 0.8 (0.4–2.3) | 1.3 (0.6–3.0) | <0.001 |
| Etiology for liver resection: | | | 0.829 |
| Hepatocellular carcinoma | 38 | 17 | |
| Metastatic liver tumor | 26 | 9 | |
| Colangiocellular carcinoma | 6 | 1 | |
| Benign liver disease | 6 | 3 | |
| Other malignant tumor | 5 | 1 | |
| Liver cirrhosis | 29 (35.8%) | 12 (38.7%) | 0.828 |
| Anemia | 12 (14.8%) | 11 (35.5%) | 0.020 |
| Diabetes mellitus | 17 (21.0%) | 13 (41.9%) | 0.033 |
| Respiratory disorder | 17 (21.0%) | 13 (41.9%) | 0.033 |
| Ischemic cerebrovascular disease | 4 (4.9%) | 5 (16.1%) | 0.112 |
| Alcohol abuse | 22 (21.0%) | 15 (48.4%) | 0.044 |
| Operation time, min | 195 (76–641) | 201 (76–604) | 0.810 |
| Blood loss, mL | 190 (5–2790) | 255 (5–1630) | 0.493 |
| Operative method, anatomical/limited | 32/49 | 17/14 | 0.201 |
| Non-laparoscopic surgery | 51 (63.0%) | 26 (84.0%) | 0.041 |

Data are number of patients, or median and range
AFI: abdominal wall fat index, BMI: body mass index.

**Table 2.** Results of multivariate regression analysis

| Predictors of postoperative delirium | OR | 95%CI | p-value |
|---|---|---|---|
| Age | 1.189 | 1.081–1.309 | <0.001 |
| AFI | 14.904 | 3.072–72.319 | <0.001 |
| Anemia | 1.811 | 0.481–6.815 | 0.38 |
| Diabetes mellitus | 1.014 | 0.301–3.417 | 0.982 |
| Respiratory disorder | 0.734 | 0.130–4.134 | 0.726 |
| Alcohol abuse | 2.405 | 0.678–8.534 | 0.175 |
| Non-laparoscopic surgery | 5.496 | 1.237–24.413 | 0.025 |

The multivariate analysis demonstrated that the AFI had a high OR for postoperative delirium. To determine an accurate cut-off value of AFI to be used as a risk factor for postoperative delirium, we performed an ROC analysis. The area under the ROC curve was 0.806 (95%CI 0.713–0.896) with a calculated optimal cut-off value of 1.0 for the AFI (Fig. 2).

## Discussion

Our analyses of 112 patients revealed that the independent risk factors of postoperative delirium after liver resection were advanced age, high AFI, and non-laparoscopic surgery. The AFI in particular showed the highest odds ratio for the occurrence of postoperative delirium. Several studies dem-

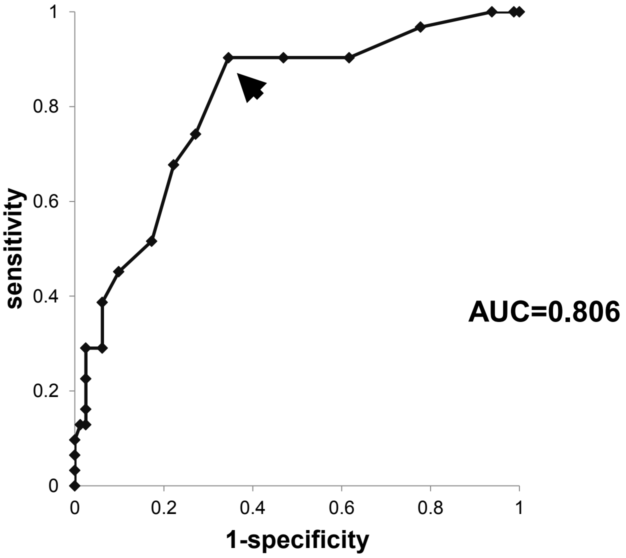

**Figure 2.** Receiver-operating characteristic (ROC) curve showing the optimal cut-off value of AFI to be used as a risk factor for postoperative delirium. *Arrow*: The optimal cut-off point.

onstrated that the AFI is a useful parameter for evaluating metabolic disorders and atherosclerosis (16–19). The AFI is also described as a significant factor for predicting risk factors of disorders of metabolism and atherosclerosis such as advanced age, smoking, high systolic blood pressure, and hyperlipidemia in non-obese men (18). Kawamoto et al. (16) reported that the AFI was an important factor for assessing visceral fat accumulation. The distribution of the body fat is an important factor in metabolic disorders and atherosclerosis. Visceral fat accumulation is more closely associated with metabolic disorders and atherosclerosis than subcutaneous fat or total mass of body fat (20).

In contrast, several reports described that atherosclerosis is an important risk factor for postoperative delirium (12–15). Otomo et al. (13) reported that postoperative delirium was associated with pre-existing cerebral infarctions and ascending aortic atherosclerosis in elderly patients who underwent coronary artery bypass graft surgery. Rudolph et al. (15) reported that vascular risk factors including hypertension, diabetes, smoking, and the need for vascular surgery are useful predictors to identify patients at high risk for postoperative delirium. These findings suggest that elevated an AFI is a good candidate for a predictor of postoperative delirium. Previous studies examined the AFI using ultrasonography (US) (16–19). In the present study, we used CT to calculate the AFI. A CT examination entails radiation exposure, unlike US. However, in patients who will undergo a liver resection, a CT examination is always needed in order to evaluate liver lesions and the anatomy of the liver. No additional CT is required to evaluate and calculate these patients' AFI.

Our present findings demonstrated that conventional open surgery was an independent risk factor for postoperative delirium. Several reports describe that systemic stress and the inflammatory response play important roles in the pathogenesis of postoperative delirium (21, 22). Moreover, the serum levels of inflammatory biomarkers such as interleukin-6 (IL-6) were reported to be positively correlated with the occurrence of postoperative delirium (23, 24). Lee et al. (23) proposes that high levels of serum IL-6 at 24-hr after surgery may be a useful predictor for postoperative delirium. Several studies have shown that laparoscopic liver resection reduced the inflammatory response including the elevation of the serum IL-6 level compared with open liver resection (25).

Pain intensity after surgery is a candidate risk factor for the development of postoperative delirium in elderly surgical patients (26). Interestingly, Behrends et al. (27) reported that intraoperative blood transfusion of >1,000 ml of erythrocyte concentrates was a significant risk factor for postoperative delirium. Laparoscopic surgery is less invasive compared to conventional open surgery because of its minimal abdominal wall incision, less intraoperative blood loss, and reduced postoperative pain. These findings suggest that minimally invasive surgery including laparoscopic surgery may contribute to the prevention of postoperative delirium in patients undergoing liver resection.

In our study, advanced age was revealed as another candidate risk factor for postoperative delirium. Several other studies have demonstrated that advanced age was a well-established risk factor of postoperative delirium (1–6). Our present results showed that the patients in the delirium group were approx. 8 years older on average than those in the non-delirium group. Yoshimura et al. (9) reported that all delirious patients who underwent liver resection for HCC were >65 years old. An advanced age is involved in various risks of postoperative delirium such as atherosclerosis, ischemic cerebrovascular disease, hypoalbuminemia, and metabolic disorders (1–6, 28). The number of elderly patients needing liver resection could be increasing due to the increasing life expectancy in many countries. Therefore, we recommend routine systematic screening prior to liver resection to detect risk factors in elderly patients for the prevention of postoperative delirium.

Postoperative delirium is associated with not only higher morbidity, longer length of hospitalization, and higher healthcare costs but also higher mortality. Moskowitz et al. (29) reported that postoperative delirium was independently associated with a seven-fold increase in 5-year mortality. The importance of the team-based approach including anesthesiologists, psychiatrists, nurses, and pharmacists was recently proposed to prevent postoperative delirium (30).

In conclusion, this is the first report that the AFI is the most useful predictor for postoperative delirium after liver resection. Elderly patients with a higher AFI (>1.0) and open liver resection are associated with an increased risk of postoperative delirium. The determination of patients' AFI values will help identify patients at high risk for postoperative delirium and help prevent postoperative delirium by team-based intervention.

**Conflict of interest**: None declared.

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