論文・抄録

The Benefits of a Wound Protector in Preventing Incisional Surgical Site Infection in Elective Open Digestive Surgery: A Large-Scale Cohort Study

ORIGINAL SCIENTIFIC REPORT

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Abstract

Background: The objective of this study was to evaluate the benefits of wound protectors (WPs) in preventing incisional surgical site infection (I-SSI) in open elective digestive surgery using data from a large-scale, multiinstitutional cohort study.

Methods: Patients who had elective digestive surgery for malignant neoplasms between November 2009 and February 2011 were included. The protective value of WPs against I-SSI was evaluated.

Results: A total of 3201 patients were analyzed. A WP was used in 1022 patients (32%). The incident rate of I-SSI(not including organ/space SSI) was 9%. In the univariate and the multivariate analyses for perioperative risk factors for I-SSI, the use of WP was an independent favorable factor that reduced the incidence of I-SSI (odds ratio 0.73, 95% confidence interval 0.55–0.98. $P = 0.038$). The subgroup forest plot analyses revealed that WP reduced the risk of I-SSI only in patients aged 74 years or younger, males, non-obese patients (body mass index <25 kg/m^2), patients with an American Society of Anesthesiologists score of 1/2, patients with a previous history of laparotomy, nonsmokers, and patients who underwent colon and rectum operations. In patients who underwent colorectal surgery, the postoperative hospital stay was significantly shorter in patients with WP than those without WP (median 13 vs. 15 days, $P = 0.040$). In terms of the depth of SSI, WP only prevented superficial I-SSI and did not reduce the incidence of deep I-SSI.

Conclusions: WP is a useful device for preventing superficial I-SSI in open elective digestive surgery.

Trial registration number: UMIN000004723.

Abbreviations

ASA	American Society of Anesthesiologists
BMI	Body mass index
CT	Computed tomography
CI	Confidence interval
DI-SSI	Deep incisional surgical site infection
HBP	Hepato-biliary-pancreatic
I-SSI	Incisional surgical site infection
OR	Odds ratio
OS-SSI	Organ/space surgical site infection
SI-SSI	Superficial incisional surgical site infection
WP	Wound protector

Introduction

An incisional surgical site infection (I-SSI) is one of the common postoperative morbidities after digestive surgery [1–3]. The incidence of I-SSI increases not only the cost of treatment but also the risk of incisional hernia as a long-term complication [4]. Previous studies have reported numerous independent risk factors for I-SSI. The improvement in intraoperative wound management is one of the most important methods for reducing I-SSI [1–3, 5–7]. Intraoperative wound management has been reported to have an impact on the incidence of I-SSI and includes the use of antibiotic prophylaxis [1, 2, 5], skin preparation [1, 2, 5, 8], skin drape [9], operative double gloving [2, 10–12], body temperature [2, 13], wound length [7], subcutaneous lavage before closure [14–16], subcutaneous drainage [17–19], methods of skin suture (subcuticular absorbable suture) [5, 17, 20, 21], and skin wound dressing [22].

Generally, I-SSI is associated with a number of local bacteria [23, 24]. In an experimental mouse model, 10^5 bacteria in 1 g of tissue is sufficient to induce I-SSI [23]. To reduce the incidence of I-SSI, it is necessary to prevent surgical wound exposure to bacteria. In this regard, the use of a wound protector (WP) during the operation is thought to protect against exposure to bacteria, especially enteric bacteria, on the wound edge while performing gastrointestinal surgery [24, 25]. In fact, the latest guidelines recommend the use of a WP as for the prevention of I-SSI (evidence level I) [2].

Although several randomized control trials [26–31] and meta-analyses [32–36] have reported that WP reduced the incidence of I-SSI, these trials had a small number of patients ($n = 64$–729), and there is no prospective, large-scale (more than 1000 patients) study of the clinical value of WPs. In this study, the data from a prospective and large-scale multi-institutional cohort study (including more than 3000 patients) were used to evaluate the clinical value of WPs for I-SSI in open elective digestive surgeries for malignant neoplasms.

Methods

Patients:

This study analyzed the data from a subset of patients enrolled in a prospective observational study for incisional hernia and incisional surgical site infections [4, 7]. The main protocol was approved by the institutional review boards of Nagoya University Graduate School of Medicine and the participating hospitals, and the study design was registered with the Infrastructure for Academic Activities with the University Hospital Medical Information Network Identifier (UMIN000004723, http://www.umin.ac.jp/ctr/index/htm). Informed consent was obtained from each patient before enrollment in the study.

In this cohort, patients who underwent open abdominal surgery between November 2009 and February 2011 at Nagoya University Hospital and the 19 affiliated hospitals were enrolled. The eligibility criteria for this study were as follows: (1) 20 years or older; (2) open (not laparoscopic) intraabdominal digestive organ (the stomach, colorectal, liver, gallbladder, bile duct, and pancreas) resections for malignant tumors; (3) no incision other than in the abdomen or perineum; and (4) no artificial implantation. Patients who underwent laparoscopic or laparoscopy-assisted surgeries were excluded. Patients without tumor resection (e.g., bypasses of the digestive tract and exploratory laparotomies) were also excluded.

Monitored perioperative factors:

Clinical data, including preoperative, intraoperative, and postoperative factors, were prospectively recorded by the surgeons who were in charge of data collection at each hospital. Prospectively monitored preoperative clinical data included age, gender, body mass index (BMI), American Society of Anesthesiologists (ASA) score, previous medical history (laparotomy and chemotherapy), smoking status, and subcutaneous fat thickness. Subcutaneous fat thickness was preoperatively measured with computed tomography (CT) at the thickest incisional location.

Prospectively monitored intraoperative factors included operative procedure (stomach, colon and rectum, or hepato-biliary-pancreatic surgeries), operative time, blood loss, wound length, intraoperative allogeneic blood transfusion, type of incision (midline/pararectal/transverse/inverted L/Mercedes), the use of a WP, subcutaneous lavage, the type of skin closure, and skin wound dressing.

The protection method of the wound edge was freely chosen according to the policy of each institution or surgeon. In this study, only patients with plastic WPs were included in the WP group. Other patients who were operated on with cloth towel wound coverage or no coverage were included in the no-WP group. The plastic WP was either the dual ring WP (Alexis™ wound, Applied Medical Resources Corporation) or the single ring WP (Steri-Drape™ Wound Edge Protector, 3 M Health Care).

The endpoint of this study was to evaluate the clinical value of WPs in preventing the incidence of I-SSI (not including organ/space SSI, OS-SSI). Only the condition of the abdominal wound was used for the data analysis. The Centers for Disease Control and Prevention definitions of SSI were employed when monitoring the incidence of I-SSI [1]. I-SSI included both superficial incisional surgical site infection (SI-SSI) and deep incisional surgical site infection (DI-SSI). SI-SSI was diagnosed when the incidence occurred within 30 days after the operation and involved the skin and subcutaneous tissue with one of the following conditions: (1) purulent discharge; (2) organisms isolated from an aseptically obtained culture of

fluid or tissue; (3) signs or symptoms of infection, including pain/tenderness, localized swelling, redness/heat, and an open wound; or (4) diagnosis of SI-DDI by a surgeon or attending physician [1]. DI-SSI was diagnosed when the infected wound involved fascial and muscle layers but not the organ space [1].

Data collection and follow-up:

After surgery, patients were monitored daily during their hospital stay, and all perioperative data were prospectively recorded in a database. After discharge, patients were followed up for at least 30 days in an outpatient clinic.

Statistical analysis:

In the univariate analysis, differences among categorical variables were analyzed using the Chi-square test. The logistic regression model (stepwise forward) was used to calculate the odds ratio (OR) with 95% confidence intervals (CIs). In the multivariate analysis, all possible risk factors were evaluated for the analysis. A subgroup analysis for the incidence of I-SSI was calculated with Fisher's exact test. *P* values of less than 0.050 were considered statically significant. The data analysis was performed using IBM SPSS statistical software (version 21; SPSS Japan Inc.).

Results

Clinical characteristics of the study patients:

Between November 2009 and February 2011, a total of 4305 consecutive patients were enrolled in the main study: a prospective monitoring program for the incidence of incisional hernia in abdominal surgery [4]. Among them, 3201 patients fulfilled the eligibility criteria of this study (Table 1). The median follow-up period was 461 days (range 2–1105), and a total of 3113 patients (97%) were followed up for 30 or more days. The follow-up period was less than 30 days in 88 patients (3%) because of the loss of revisits in the outpatient department (n = 42), reoperation (n = 38), and postoperative death (n = 8).

Table 1 Clinical characteristics of the patients (n = 3201)

Factors	*N* (%) or median [interquartile range]
Preoperative factors	
Age (years old)	69 [62–76]
Gender	
Male	2101 (66%)
Female	1100 (34%)
Body mass index (kg/m^2)	21.9 [19.7–24.2]
American Society of Anesthesiologists score	
1	1319 (41%)
2	1742 (54%)
3	137 (4%)
4	13 (1%)
Previous history of laparotomy	753 (24%)
Preoperative chemotherapy	208 (6%)
Smoking within 1 month	753 (24%)
Subcutaneous fat thickness by CT (cm)	1.7 [1.2–2.3]
Operative factors	
Operative procedure	
Stomach	993 (31%)
Colon and rectum	1439 (45%)
Hepato-biliary-pancreatic	769 (24%)
Operative time (min)	199 [145–281]
Blood loss (ml)	290 [120–663]
Wound length (cm)	19 [15–23]
Intraoperative allogeneic blood transfusion	367 (9%)
Type of incision	
Midline	2605 (81%)
Pararectal	144 (5%)
Transverse	48 (1%)
Inverted L	330 (11%)
Mercedes	74 (2%)
Wound protector	1022 (32%)
Subcutaneous lavage	2331 (73%)
Type of skin closure	
Interrupted transdermal suture	1346 (42%)
Subcuticular suture	1855 (58%)
Skin wound dressing	1447 (45%)
Postoperative complications	
All complications	977 (31%)
Surgical site infections	644 (21%)
Incisional surgical site infection	280 (9%)
Superficial incisional surgical site infection	229 (7%)
Deep incisional surgical site infection	51 (1%)
Organ/space surgical site infection	410 (13%)
Remote infection	202 (6%)
In-hospital death	21 (1%)
Postoperative hospital stay (day)	14 [2–255]

Table 2 Univariate analyses of perioperative risk factors for I-SSI (n = 3201)

Factors	*N*	No. of I-SSI (%)	*P* value
Preoperative factors			
Age (years old)			0.312
≦74	2223	187 (8)	
≧75	978	93 (9)	
Gender			0.870
Male	2101	185 (8)	
Female	1100	95 (8)	
Body mass index (kg/m^2)			0.040
<25.0	2594	218 (8)	
≧25.0	607	62 (10)	
ASA score			0.018
1/2	3061	260 (9)	
3/4	140	20 (14)	
Previous history of laparotomy			0.002
Absent	2448	193 (8)	
Present	753	87 (12)	
Preoperative chemotherapy			0.578
Absent	2993	264 (9)	
Present	208	16 (8)	
Smoking (within 1 month)			0.502
Absent	2963	262 (9)	
Present	238	18 (8)	
Subcutaneous fat thickness by CT(cm)			0.034
<3.0	2998	254 (9)	
≧3.0	203	26 (13)	
Operative factors			
Operative procedure			<0.001
Stomach	993	28 (3)	
Colon and rectum	1439	174 (12)	
Hepato-biliary-pancreatic;	769	78 (10)	
Operative time (h)			0.002
<4.0	2089	160 (8)	
≧4.0	1112	120 (11)	
Blood loss (ml)			0.005
<500	2136	166 (8)	
≧500	1065	114 (11)	
Wound length (cm)			<0.001
<20.0	2099	142 (7)	
≧20.0	1102	138 (13)	
Intraoperative allogeneic blood transfusion			0.160
Absent	2834	241 (9)	
Present	367	39 (11)	
Type of incision			0.200
Midline	2605	220 (8)	
Non-midline	596	60 (10)	

Table 2 continued

Factors	*N*	No. of I-SSI (%)	*P* value
Wound protector			0.028
No use	2179	207 (10)	
Use	1022	73 (7)	
Subcutaneous lavage			0.311
Absent	870	69 (8)	
Present	2331	211 (9)	
Type of skin closure			0.381
Interrupted transdermal sutures	1346	128 (10)	
Subcuticular sutures	1855	152 (8)	
Skin wound dressing			0.562
Absent	1754	158 (9)	
Present	1447	122 (8)	
Hospital size			0.004
High-volume center	1563	114 (7)	
Non-high-volume center	1638	166(10)	

ASA score American Society of Anesthesiologists score, *CI* confidence interval, *I-SSI* incisional surgical site infection, *OR* odds ratio

A WP was used in 1022 patients (32%). For the remaining 2179 patients, a cloth towel was used (n = 1868) or the wound was exposed to the air without the use of any wound coverage (n = 311). I-SSI occurred in 280 patients (9%), including 229 patients (8%) with SI-SSI and 51 patients (1%) with DI-SSI.

Among 280 patients with I-SSI, the microbiological culture from

Table 3 Multivariate analyses of perioperative risk factors for I-SSI (n = 3201)

Factors	OR (95% CI)	P value
Operative procedure		<0.001
Colon and rectum	4.72 (3.13–7.13)	<0.001
Hepato-biliary-pancreatic	2.41 (1.49–3.90)	<0.001
Wound length (cm) ≧ 20.0 cm	1.86 (1.39–2.47)	<0.001
ASA score 3 + 4	1.68 (1.01–2.80)	0.045
Operative time ≧ 4.0 h	1.54 (1.15–2.05)	0.003
Previous history of laparotomy	1.46 (1.10–1.95)	0.009
Wound protector use	0.73 (0.55–0.98)	0.038
High-volume center	0.67 (0.52–0.87)	0.003

ASA score American Society of Anesthesiologists score, *CI* confidence interval, *I-SSI* incisional surgical site infection, *OR* odds ratio

infectious site was performed in 131 patients (47%) including 43 with WP and 88 without WP. The skinderived bacteria were detected in 44 patients (13 with WP and 31 without WP). The gut-derived bacteria were detected in 85 patients (34 with WP and 51 without WP).

Univariate and multivariate analyses for perioperative risk factors for I-SSI:

Among the possible risk factors (including 8 preoperative,10 operative factors, and 1 hospital size), a total of 10 factors were significantly associated with I-SSI in the univariate analysis (Table 2). Those factors included 4 preoperative factors (high BMI, high ASA, a previous history of laparotomy, and thick subcutaneous fat by CT), 5 operative factors (colon and rectum or hepato-biliary-pancreatic surgery, a long operative time, great blood loss, a long wound length, and no use of WP), and hospital volume. All possible risk factors were included in the multivariate analysis using the logistic regression model (stepwise forward). Consequently, 7 factors were identified as being independent risk factors for I-SSI (Table 3). These factors included the operative procedure (colon and rectum, OR 4.72 and hepato-biliary-pancreatic, OR 2.41), a wound length 20 cm or longer (OR 1.86), an ASA 3/4 (OR 1.68), an operative time of 4.0 h or longer (OR 1.54), a previous history of laparotomy (OR 1.46), WP use (OR 0.73), and high-volume center (OR 0.67).

Subgroup analysis for the use of WP:

The subgroup forest plot analyses revealed a significant risk reduction in I-SSI when using WP in patients 74 years or younger, males, non-obese patients (BMI less than 25 kg/m^2), patients with an ASA of 1/2, patients with a previous history of laparotomy, non-smokers (within 1 month), patients who underwent an operation of the colon and rectum, and patients without OS-SSI (Fig. 1).

The impact of WP use on the incidence of I-SSI:

Although the use of a WP did not have an impact on the incidence of DI-SSI, it tended to reduce the incidence of SI-SSI (Table 4). In particular, the incidence of SI-SSI was significantly lower when WP was used in colon and rectum surgeries. The postoperative hospital stay was also significantly shorter when WP was used in colon and rectum surgeries.

Discussion

This study focused on the clinical value of WP use in preventing the incidence of I-SSI in open digestive surgery, including gastric, colorectal, and hepato-biliary-pancreatic surgeries. The incidence of I-SSI was 9% in all patients (8% for SI-SSI and 1% for DI-SSI). The use of a WP independently decreased the incidence of I-SSI in all digestive surgery. Subgroup analyses indicated that the use of a WP significantly reduced the incidence of SI-SSI in colorectal surgery.

Although the latest meta-analysis [32–36] reported that WP was useful in preventing I-SSI events, no prospective large-scale (more than 1000 patients) study had investigated the clinical value of WPs. The number of patients included in this study was equal to or more than the sample size of recently published meta-analyses (n = 939–3695) [32–36]. Moreover, in this cohort, almost all

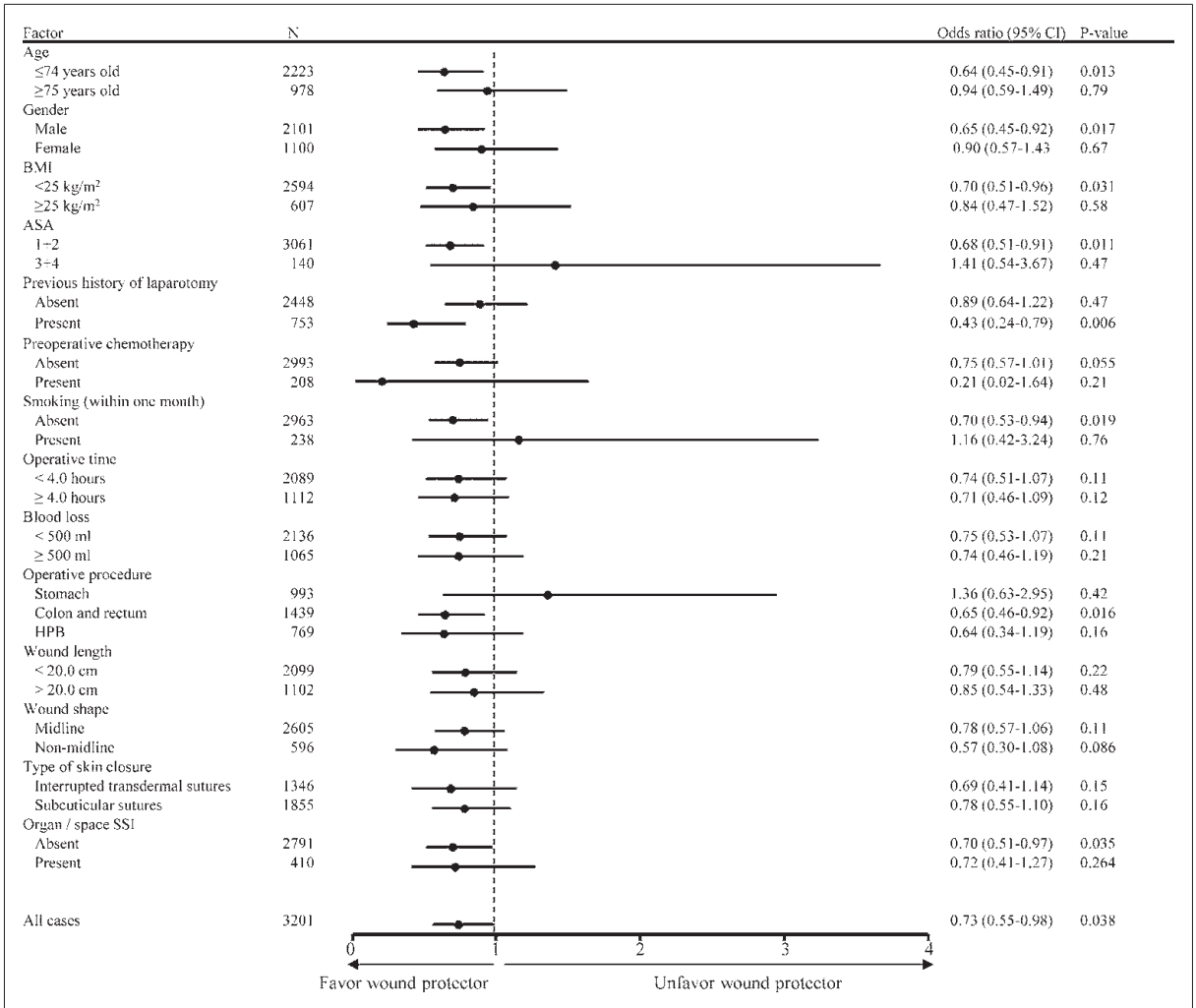

Fig. 1 A forest plot of the subgroup analyses for the use of a wound protector in preventing incisional surgical site infection (I-SSI). *ASA* American Society of Anesthesiologists, *BMI* body mass index, *CI* confidence interval, *HBP* hepato-biliary-pancreatic

Table 4 Relationship between the use of a wound protector and the depth of incisional surgical site infection/length of postoperative hospital stay

	All patients			Colon and rectum		
	Wound protector,*n*		*P* value	Wound protector,*n*		*P* value
	No use, 2179	Use, 1022		No use, 915	Use, 524	
I-SSI						
Absent	1972 (91%)	949 (93%)	0.059	800 (86%)	475 (91%)	0.040
SI-SSI	172 (8%)	57 (6%)		106 (12%)	39 (7%)	
DI-SSI	35 (1%)	16 (1%)		19 (2%)	10 (2%)	
Postoperative hospital stay (days)	15 (2–255)	15 (6–182)	0.23	15 (2–255)	13 (6–135)	<0.001

DI-SSI deep incisional surgical site infection, *SI-SSI* superficial incisional surgical site infection

patients (97%) were followed up for more than 30 days, and I-SSI after discharge was also evaluated at the outpatient clinic. This cohort was useful in evaluating the clinical impact of WP use in abdominal surgery.

The use of a WP protects the incisional site from bacteria [24, 25]. The bacteria that may contaminate the surgical wound are classified into two categories: skin bacteria (e.g., Staphylococcus aureus) and enteric bacteria (e.g., Escherichia coli). A previous study (about bacterial colonization on the surface of WP in open gastrointestinal surgery) reported that the frequency of positive bacterial cultures was significantly lower on the outside surface of the WP (incisional skin site) than that on the inside surface of the WP (abdominal cavity) [25]. The same study also demonstrated that the use of a WP significantly reduced wound exposure to enteric bacteria (not skin-derived bacteria), especially in colorectal surgery [25]. The subgroup analyses of this study and other studies [29–31] also demonstrated that the use of a WP decreased I-SSI, especially SI-SSI, in open colorectal surgery. The microbiological culture of this study detected the bacteria derived from both skin and gut. The gut-derived bacteria were detected approximately 80% (24 out of 43) in the patients who developed I-SSI in the WP group. These results indicated that the WP usage was not adequate to avoid the bacterial contamination from the gut and that the other intraoperative procedures and techniques are necessary to further prevent I-SSI.

In this study, only patients for whom plastic WP was used during the operation were included in the WP group. Patients who had a cloth towel used for wound coverage were included in the no-WP group. Although there was no significant difference in the incidence of I-SSI between the patients with no wound coverage (10%) and those with cloth towel coverage (9%), the patients with plastic WP had a significantly lower incident rate of I-SSI (7%) than the other two groups. These results correspond with the observation in a previous randomized controlled study comparing the group with intraoperative wound coverage with WP and that with a surgical towel [31]. It is speculated that the contaminated exudates during surgery may infiltrate the cloth towel and reach the wound edge, thus leading to the higher incidence of I-SSI. Therefore, the use of a cloth towel is not recommended for covering the wound edge [31].

Almost all previous studies on the incidence of SSI did not differentiate the depth of the SSI (i.e., SI-SSI and DI-SSI). Only this study and the latest meta-analysis demonstrated that the use of WP reduced the incidence of SI-SSI rather than that of DI-SSI [36]. The results in this study imply that the use of WP is not effective in preventing the incidence of deep layer wound infection. Further investigations are necessary to identify wound management methods to prevent the incidence of DI-SSI.

The use of a WP reduced not only the incidence of I-SSI but also the length of the postoperative hospital stay in colorectal surgery patients. The prevention of the incidence of I-SSI may also reduce the cost for wound management such as drainage, bacterial culture, antibiotics use, and others. In our institution, the average length of hospital stay after colorectal surgery is approximately 15 days, and the average daily cost for a hospital stay, excluding the surgery- related costs, is approximately $360. The average hospital stay was 2 days shorter in patients with WP use compared to those without WP use. The cost of a WP is approximately $80. Therefore, the use of WP may have the potential to save approximately $640 (=360 × 2 – 80) of medical costs per patient.

The subgroup analyses demonstrated that WP had a favorable effect in preventing I-SSI in the groups of younger age 74 years or less, no obesity (BMI less than 25 kg/m^2), with an ASA 1/2, absent of previous history of laparotomy, and who were non-smokers (within 1 month). Those groups were thought to be of low risk of I-SSI. In high risk groups for I-SSI (e.g., older age, obesity, and an ASA of 3/4), the use of a WP may not be sufficient for preventing the incidence of I-SSI. In terms of type of SSI, although the WP usage reduced the incidence rate of I-SSI among the patients without concomitant OS-SSI, it did not reduce the incidence of I-SSI in patients with OS-SSI. It is speculated that the effect of WP is modest, and an additional preventive treatment is required to reduce the incidence of I-SSI in patients with concomitant OS-SSI.

Other independent risk factors for I-SSI identified by the multivariate analysis included a high ASA score, a previous history of laparotomy, operative procedures (colorectal and hepato-biliary-pancreatic surgery), operative time, and the wound length. However, these factors are generally unchangeable because they are determined by the patients' condition, including their disease status. The use of WP is the only factor that can be managed by the surgeon's ingenuity.

There are several limitations in this study. The primary endpoint of the original study was the rate of incisional hernia after abdominal surgery [4], and this study was thought to be a secondary post hoc analysis. Nevertheless, the number of registered patients in this study is equal to the number in the latest meta-analyses [33, 34, 36]; thus, the results are meaningful. Another limitation is that this study was not a randomized controlled trial and that the use of WP was depending on institutional policy or surgeon's preference. Therefore, we performed a sensitivity analysis in addition to the main analysis to offset the limitation of variable WP usage rate among institutions. Consequently, it was evident that the use of WP was valuable in reducing the incidence of I-SSI.

Conclusion

The WP is a useful device for preventing I-SSI in open elective digestive surgery.

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Compliance with ethical standards:

Conflicts of interest From October 2009 to September 2013, Ethicon Japan KK paid Nagoya University Graduate School of Medicine through the endowed chair's (The Division of Surgical Infection) employment of Keita Itatsu, Yukihiro Yokoyama, and Gen Sugawara. The other authors had no conflicts of interest.

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The Impact of the Location of Esophagogastrostomy on Acid and Duodenogastroesophageal Reflux After Transthoracic Esophagectomy with Gastric Tube Reconstruction and Intrathoracic Esophagogastrostomy

ORIGINAL SCIENTIFIC REPORT

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Abstract

Background: The aim of this study was to evaluate the impact of the location of esophagogastrostomy on acid and duodenogastroesophageal reflux (DGER) in patients undergoing gastric tube reconstruction and intrathoracic esophagogastrostomy.

Methods: Thirty patients receiving transthoracic esophagectomy without cervical lymph node dissection and gastric tube reconstruction by intrathoracic anastomosis were enrolled. All patients underwent 24-h pH and bilirubin monitoring and gastrointestinal endoscopy one year after surgery. Patients were divided into three groups according to esophagogastrostomy location: group A (n = 9), above the top of the aortic arch; group B (n = 15), between the top and bottom of the aortic arch; and group C (n = 6), below the bottom of the aortic arch. The relations among the esophagogastrostomy location, 24-h pH and bilirubin monitoring results, endoscopic findings, and reflux symptoms were investigated.

Results: No acid reflux into the remnant esophagus was observed in group A, whereas it was observed in three of 15 patients (20%) in group B and in two of six patients (33%) in group C (P = 0.139).

No DGER was found in group A, whereas DGER was observed in eight (53%) patients in group B and all patients in group C (P<0.001). Reflux esophagitis was observed in one patient (11%) in group A, five patients (33%) in group B, and all patients in group C (P = 0.002).
Conclusion: In gastric tube reconstruction via intrathoracic anastomosis, esophagogastrostomy should be performed above the top of the aortic arch to prevent postoperative DGER and reduce the incidence of reflux esophagitis.

Introduction

Postoperative reflux esophagitis can greatly decrease patient quality of life. In addition, this condition is the main risk factor related to esophageal adenocarcinoma in the remnant esophagus [1]. After esophagectomy and gastric tube reconstruction, there is no structure preventing gastric acid reflux into the remnant esophagus or duodenogastroesophageal reflux (DGER) due to the resection of the esophagogastric junction. Therefore, a higher incidence of reflux esophagitis after esophagectomy and gastric tube reconstruction, compared with that in the general population, has been reported [2, 3]. Transthoracic esophagectomy with gastric tube reconstruction and intrathoracic esophagogastrostomy has been performed for esophageal cancer throughout the world, and there is a common theory that intrathoracic esophagogastrostomy should be performed at the high position. However, only a few reports support this theory on the basis of endoscopic findings [4, 5]. Furthermore, there are no detailed studies comparing the location of esophagogastrostomy and the extent of acid reflux and DGER in patients who underwent intrathoracic esophagogastrostomy.

The aim of this study was to evaluate the impact of the location of esophagogastrostomy on acid reflux and DGER in patients undergoing gastric tube reconstruction and intrathoracic esophagogastrostomy.

Materials and methods

Patients: One hundred and forty patients underwent transthoracic esophagectomy for esophageal cancer in our department between January 1997 and December 2011. Of them, 66 patients received gastric tube reconstruction and intrathoracic esophagogastrostomy. Twenty-six patients with cervical lymph node dissection were excluded from this study because cervical lymph node dissection causes skin flap adhesions or anterior cervical muscle scarring, which prevent the elevation of the larynx in swallowing, thereby impairing swallowing function [6]. Ten patients who refused simultaneous pH and bilirubin monitoring were also excluded. Thus, the remaining 30 patients were subjected to analysis, which included 22 men and 8 women with a median age of 67.5 years (range 52–79 years). The patients were evaluated using simultaneous pH and bilirubin monitoring, endoscopy, and reflux symptoms.

Surgical procedure: The abdomen was explored through an upper midline incision. After perigastric and celiac lymph node dissection, the gastric tube was constructed using a linear cutting stapler (Proximate Linear Cutter 75, Ethicon Endo-Surgery, Cincinnati, OH, USA). The stapler was fired as many times as needed to divide the stomach from the lesser curvature at the anastomosis between the right and left gastric arteries along the greater curvature axis, creating an approximately 4-cm-wide tube. Digital dilatation of the pyloric ring was performed for all patients. Esophagectomy with mediastinal lymph node dissection was performed via a right (n = 28) or left (n = 2) transthoracic approach. The gastric tube was placed in the posterior mediastinum, and an intrathoracic esophagogastrostomy was performed on the anterior wall of the gastric tube using a circular stapler (CEEA 25, Medtronic, Minneapolis, MN, USA).

Symptoms: Reflux symptoms, such as pharyngeal regurgitation, cervical heartburn or pain, and thoracic discomfort-associated sleep disturbance or nocturnal cough, were assessed as follows: absent, mild (can be ignored or cannot be ignored but does not affect lifestyle), and severe (affects lifestyle, including the inability to lie flat, contributing to sleep deprivation after the administration of antacids).

Endoscopy: Preoperative endoscopy was used in all patients to confirm that the squamous epithelium in the cervical esophagus was normal and that Barrett's epithelium was absent. Postoperative endoscopy was performed less than 1 month before or after the pH and bilirubin monitoring to observe mucosal changes in all patients. Reflux esophagitis was graded according to the Los Angeles Classification System. Barrett's esophagus was classified into two groups: long-segment Barrett's esophagus (LSBE) which the presence of circular Barrett's mucosa extending longitudinally for 3 cm or more is called and short-segment Barrett's esophagus (SSBE) which the presence of circular Barrett's esophagus less than 3 cm in length or non-circular Barrett's mucosa is designated [7].

Simultaneous 24-h pH and bilirubin monitoring: Simultaneous monitoring of the esophageal pH and bilirubin levels was performed for 24 h. After an antimony catheter with pH sensors (Medtronic, Skovlunde, Denmark) was passed nasally, the proximal sensor was positioned at 2 cm above the esophagogastrostomy site. The distal pH sensor was positioned at 10 cm below the proximal sensor, thus being placed in the gastric tube. The pH information was recorded on a portable digital data recorder (Digitrapper Mark III, Medtronic). Esophageal bilirubin levels were monitored with a fiber optic sensor (Bilitec 2000, Medtronic), which was positioned at the same position as the proximal pH sensor. Data were recorded on a portable optoelectronic recorder. The pH and bilirubin data were subsequently transferred to a personal computer for analysis with EsopHagram Reflux Analysis software (Medtronic). An esophageal pH below 4.0 was defined as indicating acid reflux, while an alkaline shift was defined as an esophageal pH above 7.0. The presence of acid reflux was defined as an esophageal pH below 4.0 for more than 4.4% of the total monitoring time [8]. A bilirubin absorbance exceeding 0.14 indicated bile reflux. The presence of DGER was defined as a bilirubin absorbance exceeding 0.14 for more than 1.8% of the total monitoring time [9, 10]. Patients were instructed to follow a special low-residue liquid diet (500 ml of Ensure Liquid; Dinabot, Tokyo, Japan) three times daily at their usual mealtimes during the monitoring period. Only water was allowed in addition. Although some patients complained of nasal or pharyngeal discomfort, all of the study patients tolerated the monitoring. Although ten patients took antacid medications for gastroesophageal reflux disease before this examination, all drugs that could potentially affect gastrointestinal motility and secretion were discontinued at least one week prior to the pH and bilirubin monitoring.

Identification of the esophagogastrostomy location: The esophagogastrostomy location was identified by tracing the remnant circular staple on a computed tomography (CT) image. The 30 patients were classified into three groups according the esophagogastrostomy location: group A, above the top of the aortic arch (n = 9); group B, between the top and bottom of the aortic arch (n = 15); and group C, below the bottom of the aortic arch, (n = 6) (Fig. 1). The distances from the top of aortic arch to the esophagogastrostomy location were also measured on the CT image.

Statistical analyses: The results are expressed as the median (range). Fisher's exact test and the Mann–Whitney U test were used for the analyses as appropriate to assess differences between two groups. Fisher's exact test and the Kruskal–Wallis test were used for comparing three groups. All statistical analyses were performed using SPSS software version 21.0 J. Two-sided P values were calculated and presented. A P value of <0.05 indicated statistical significance.

Results

Patient characteristics: The patient characteristics according to esophagogastrostomy location are summarized in Table 1. Age, gender, and clinical stage were not significantly different

Table 1 Patient characteristics according to esophagogastrostomy location

Variables	Esophagogastrostomy location			P
	A(n = 9)	B(n = 15)	C(n = 6)	
Age (years)	70 (55–73)	60 (52–72)	66 (58–79)	0.095
Gender (male/female)	7/2	9/6	6/0	0.199
Thoracotomy (right/left)	9/0	15/0	4/2	0.034
Location of tumor				
Ut/Mt/Lt/Ae	1/5/3/0	0/7/8/0	0/0/1/5	<0.001
Clinical stage (UICC 7th)				
Ⅰ/Ⅱ/Ⅲ	5/0/4	6/6/3	3/1/2	0.230
Antacid medications before examination, n (%)	1 (11)	5 (33)	4 (66)	0.102

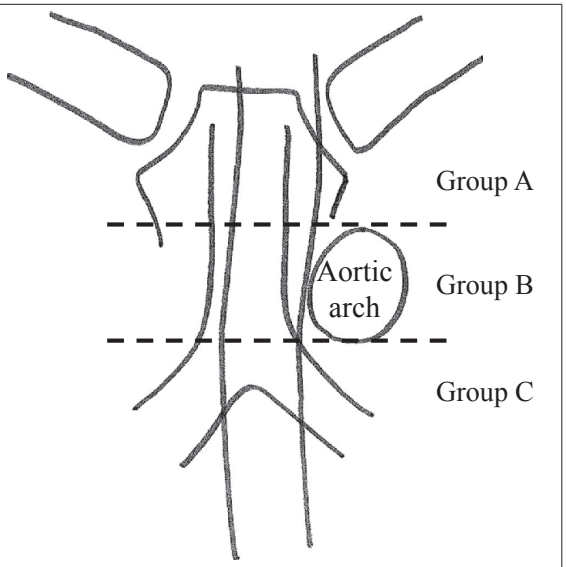

Fig. 1 Schema of the grouping method depending on the esophagogastrostomy location. *Group A*: above the *top* of aortic arch. *Group B*: between the *top* and *bottom* of aortic arch. *Group C*: below the *bottom* of aortic arch

Table 2 Relation between the esophagogastrostomy location and reflux to the remnant esophagus

Variables	Esophagogastrostomy location			*P*
	A(*n* = 9)	B(*n* = 15)	C(*n* = 6)	
Acid reflux	0	3 (20%)	2 (33%)	0.139
DGER*	0	8 (53%)	6 (100%)	<0.001

* *DGER* Duodenogastroesophageal reflux

Table 3 Relation between the esophagogastrostomy location, endoscopic findings, and reflux symptoms

Variables	Esophagogastrostomy location			*P*
	A(*n* = 9)	B(*n* = 15)	C(*n* = 6)	
Reflux esophagitis				
Present	1 (11%)	5 (33%)	6 (100%)	0.002
Mild (A or B)	0	3 (20%)	3 (50%)	
Severe (C or D)	1 (11%)	2 (13%)	3 (50%)	
Barrett's esophagus	0	4 (27%)	0	0.159
Stenosis	3 (33%)	2 (13%)	1 (17%)	0.511
Reflux symptoms				
Present	4 (44%)	9 (60%)	5 (83%)	0.437
Mild	4 (44%)	8 (53%)	4 (66%)	
Severe	0	1 (7%)	1 (17%)	

among the three groups. The thoracotomy approach (right or left) was significantly different; specifically two patients in group C underwent left thoracotomy. The tumor location was significantly different among three groups, and patients with tumors located in the abdominal esophagus were found only in group C. The esophagogastrostomy location became lower as the tumor location became lower. Though the proportion of patients with antacid medications before this examination increased as the esophagogastrostomy position became lower, there was no significant difference among three groups ($P = 0.102$).

The relations of the esophagogastrostomy location, acid reflux, and DGER: No acid reflux into the remnant esophagus was observed in group A patients, whereas acid reflux was observed in three of 15 group B patients (20%) and two of 6 group C patients (33%). There was no significant difference among the three groups ($P = 0.139$). No DGER was observed in group A patients, whereas DGER was observed in 8 of 15 group B patients (53%) and all 6 group C patients (100%). The proportion of patients with DGER increased as the esophagogastrostomy location became lower ($P < 0.001$) (Table 2).

The relations of the esophagogastrostomy location, endoscopic findings, and reflux symptoms: Reflux esophagitis was found in one patient (11%) in group A, five patients in group B (33%), and all patients in group C. The proportion of patients with reflux esophagitis increased as the esophagogastrostomy position became lower ($P = 0.002$). Half of group C patients developed

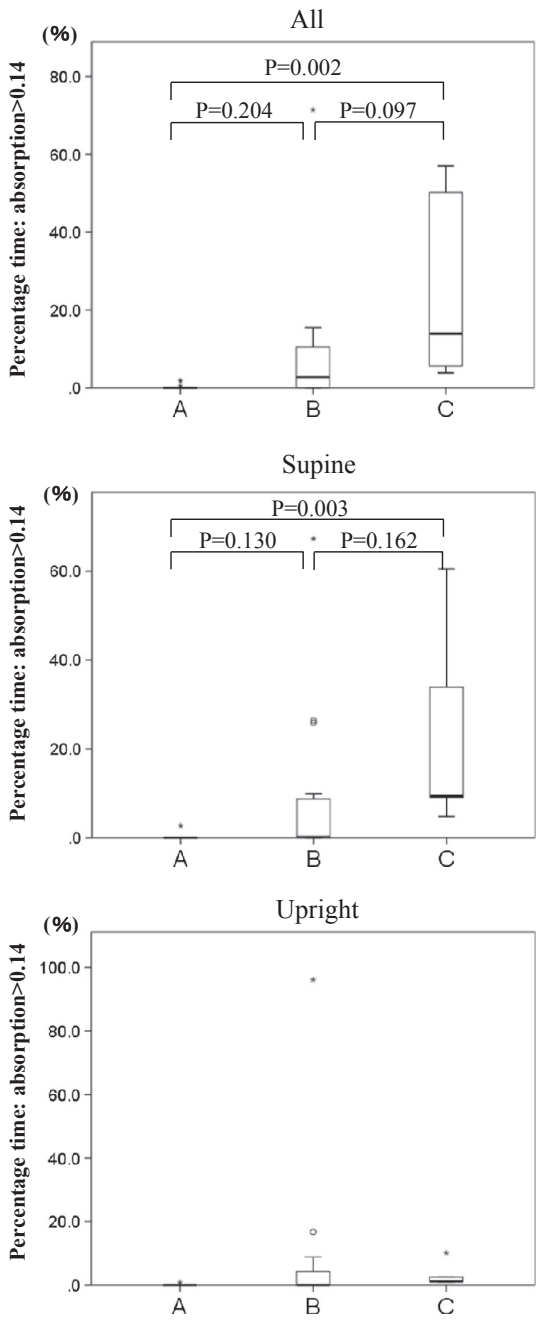

Fig. 2 Relation between the location of esophagogastrostomy and the percentage time of bile reflux

severe esophagitis. The incidence of Barrett's esophagus and stenosis was not significantly different among the three groups. Barrett's esophagus was observed in four patients of group B, and all of them had SSBE.

The incidence of reflux symptoms is likely to be associated with the esophagogastrostomy location. No patients in group A showed severe reflux symptoms, whereas one patient in both group B and group C showed severe reflux symptoms (Table 3).

The relation of the esophagogastrostomy location with acid and bile reflux into the remnant esophagus (24-h pH and bilirubin monitoring): The percentage time of bile reflux in all physical positions, the supine position, and the upright position is shown in Fig. 2. The percentage time of bile reflux in all physical positions was almost zero in group A and increased as the esophagogastrostomy position became lower ($P = 0.003$).

The percentage time of bile reflux in the supine position also increased as the esophagogastrostomy position became lower ($P = 0.004$). The percentage time of bile reflux in the upright position was near zero and similar among the three groups ($P = 0.070$). The relation between the distance from the top of the aortic arch

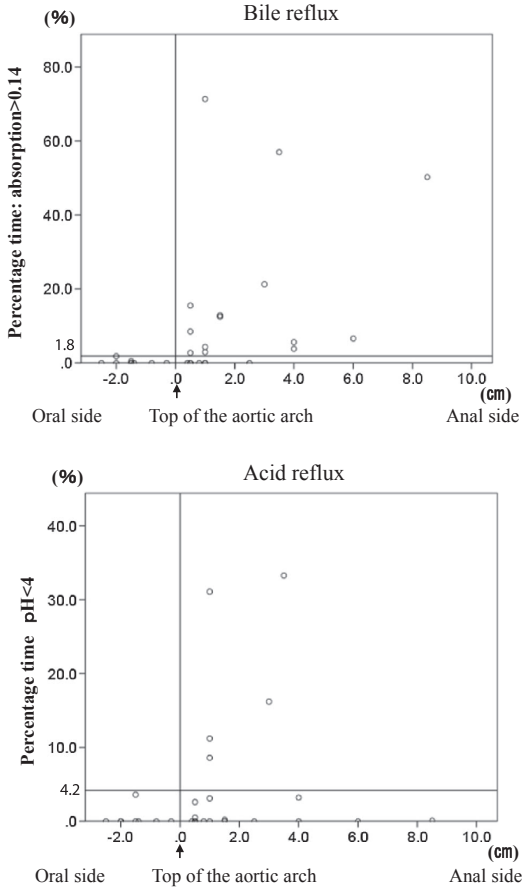

Fig. 3 Relation between the distance from the *top* of aortic arch to the esophagogastrostomy location and the percentage time of acid and bile reflux in all physical positions

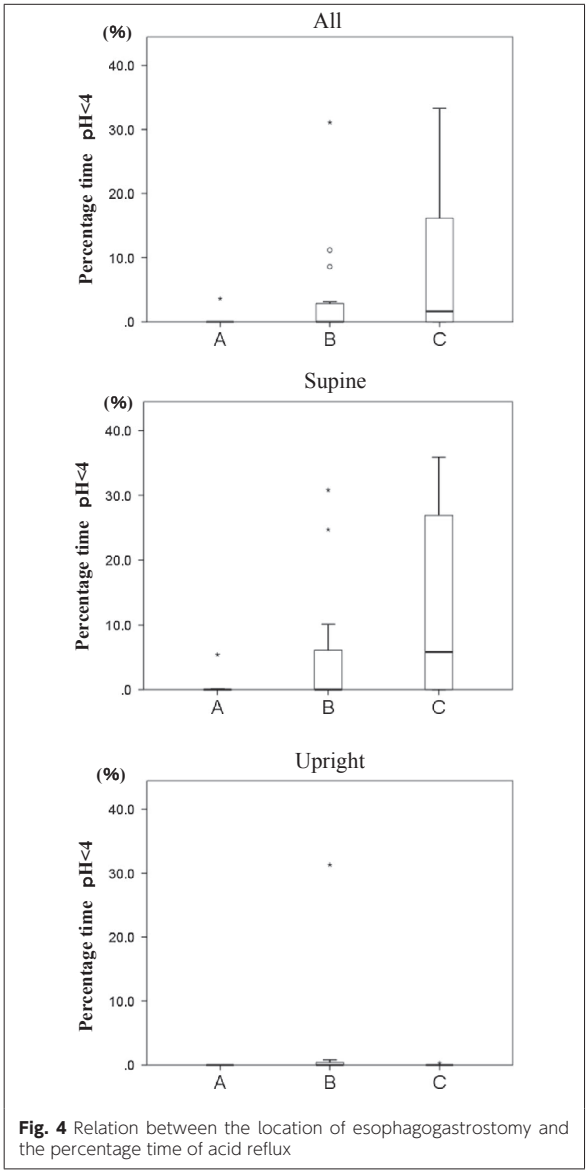

Fig. 4 Relation between the location of esophagogastrostomy and the percentage time of acid reflux

to the esophagogastrostomy location and the percentage time of acid and bile reflux in all physical positions are shown in Fig. 3. As the esophagogastrostomy location was far from the top of the aortic arch toward the anal side, the proportion of patients with bile reflux was likely to increase.

The percentage time of acid reflux in all physical positions, the supine position, and the upright position is shown in Fig. 4. Although a similar trend to bile reflux was apparent in the percentage time of acid reflux, there was no significant difference among the three groups in all physical positions, the supine position, and the upright position. There were some patients without acid reflux whose esophagogastrostomy location was more than 4 cm far from the top of the aortic arch toward the anal side (Fig. 3). The gastric acid secretory function of gastric tube may influence.

Discussion

The present study showed that the incidence of DGER, the percent time of bile reflux into the remnant esophagus, and the incidence of reflux esophagitis increased as the esophagogastrostomy location became lower, and no DGER was observed in patients whose anastomosis was above the top of the aortic arch. These results showed that the aortic arch was a watershed of DGER. There are only a few reports on the relation between the esophagogastrostomy location and reflux esophagitis. Hangs et al. reported that the incidence of reflux esophagitis and reflux symptoms was less in patients with supra-aortic anastomosis than in patients with infra-aortic anastomosis [4]. Palmes et al. reported that the incidence of reflux esophagitis was significantly higher in patients with anastomosis below than in patients with anastomosis above the azygos vein level [5]. Our objective and quantitative data using 24-h pH and bilirubin monitoring support the findings of these previous reports.

Reflux is promoted by the position of the gastric tube between the positive pressure environment of the abdominal cavity and the negative pressure environment of the thoracic cavity [11], as well as the worsening of the remnant esophageal clearance due to denervation and scarring of the secondary to upper mediastinal lymph node dissection [12]. The reasons why the extent of DGER depended on the location of esophagogastrostomy, particularly in the supine position, were presumed as follows: First, the distance of the esophagogastrostomy from the pylorus ring may be related to the extent of DEGR. Second, in healthy persons, esophageal peristaltic wave pressure following swallowing becomes lower as the measured location becomes further from the pharynx and is lowest at the transition point, which is approximately 7 cm away from the upper esophageal sphincter [13]. The remnant esophageal clearance may improve due to higher peristaltic pressure as the esophagogastrostomy location nears the pharynx. Third, because a longer remnant esophagus without peristalsis due to upper mediastinal lymph node dissection can cause less favorable esophageal clearance, the length of the denervated remnant esophagus may be related to the extent of DGER. Fourth, the lowest position of the esophagus is generally around the level of the bifurcation of the trachea in the supine position, and there is a downward slope from the upper thoracic esophagus to the middle thoracic esophagus. As the esophagogastrostomy location approaches the top of the slope, reflux into the remnant esophagus becomes more difficult.

In our study, the esophagogastrostomy location became lower as the tumor location became lower. Surgeons usually mind whether the reconstructed gastric tube sufficiently reaches the remnant esophagus; thus, they are likely to leave long segments of remnant esophagus without peristalsis. This concern may be biased, and esophagogastrostomy should be performed as high as possible regardless of the tumor location.

An esophagogastrostomy via a left thoracotomy must be

performed below the bifurcation of the trachea, i.e., at the lowest position of the esophagus in the supine position. In our one patient with abdominal esophageal cancer who had undergone a left transthoracic esophagectomy and esophagogastrostomy below the bifurcation of the trachea, duodenal diversion with Roux-en Y reconstruction was required to prevent DGER due to refractory reflux esophagitis and reflux symptoms. Even for lower thoracic and abdominal esophageal cancer, an esophagectomy via a left thoracotomy and gastric tube reconstruction without an anti-reflux procedure should not be performed.

There are several limitations in this study. First, this was a retrospective study that included only a small number of patients. Second, because antacids were discontinued at least one week before the pH and bilirubin monitoring, they did not influence the pH and bilirubin monitoring results. However, they may have influenced the incidence of reflux esophagitis and reflux symptoms; the true incidence of reflux esophagitis and reflux symptoms might have been higher. Third, reflux is attributed to the balance of pressure, namely swallowing pressure, the peristaltic pressure of the remnant esophagus, the negative pressure of the thoracic cavity, and the positive pressure of the abdominal cavity. Therefore, high-resolution manometry testing is needed to investigate further details of reflux mechanisms. Fourth, this study follow-up is short, as we performed this examination only one year after esophagectomy. Yajima et al. [14] reported that the cumulative incidence of reflux esophagitis was 24% at 5 years after surgery and 60% at 10 years. The reasons why such phenomenon happened are supposed to be that a denervated stomach as an esophageal substitute can recover to a normal pH profile with time, as Gutschow et al. [15] and Romagnoli et al. [16] reported, and that the remnant esophageal clearance can worsen due to impairment of swallowing function by aging. The results of this study may depend on the timing of the evaluation. The evaluation including endoscopy, pH and bilirubin monitoring, and manometry is necessary at 3, 5, and 10 years after esophagectomy.

Despite the limitations of the current study, we conclude that esophagogastrostomy should be performed above the top of the aortic arch to prevent postoperative DGER and reduce the incidence of reflux esophagitis in gastric tube reconstruction via intrathoracic anastomosis.

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Tracheoesophageal fistula after total resection of gastric conduit for gastro-aortic fistula due to gastric ulcer

CASE REPORT Open Access

Sakatoku et al. Surgical Case Reports (2017) 3:90
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Abstract

Background : Tracheoesophageal fistula (TEF) is a rare but life-threatening complication after esophagectomy. It has a high mortality rate and often leads to severe aspiration pneumonia. Various types of surgical repair procedures have been reported, but the optimal management of TEF is challenging and controversial. Treatment should be individualized to each patient.

Case presentation : A 66-year-old female underwent transthoracic esophagectomy with gastric tube reconstruction and an intrathoracic anastomosis for esophageal cancer. Three years later, she had hematemesis and was diagnosed with a gastro-aortic fistula due to a gastric ulcer. She underwent endovascular aortic repair urgently at another hospital. Two days later, she underwent total resection of the gastric tube, during which time an injury to the trachea occurred; it was repaired by patching the stump of the esophagus to the injury site. Two months later, descending aortic replacement was performed due to infection of the stent graft. Six months after the first operation, a TEF developed. The patient was referred to our hospital for further treatment. The fistula was ligated and divided via a cervical approach, and a pectoralis major muscle flap was used to cover the defect. Esophageal reconstruction with the pedunculated jejunum was performed via a subcutaneous route. The postoperative course was uneventful. The patient was discharged after 6 months of physical and dysphagia rehabilitation.

Conclusion : A TEF located near the cervicothoracic border was successfully treated with a pectoralis major muscle flap through a cervical approach. Total resection of a gastric conduit in the posterior mediastinum carries a risk of tracheobronchial injury; however, if such an injury occurs, surgeons should be able to repair the injury using a suitable flap depending on the injury site.

Keywords : Tracheoesophageal fistula, Gastric conduit ulcer, Pectoralis major muscle flap

Background

Tracheoesophageal fistula (TEF) is a rare but lifethreatening complication after esophagectomy. It has a high mortality rate and often leads to severe aspiration pneumonia [1, 2]. Various types of surgical repair procedures have been reported, but the optimal management of TEF is challenging and controversial. Treatment should be individualized to each patient. Herein, we report a patient with a TEF after total resection of a gastric conduit for gastro-aortic fistula due to a gastric ulcer, successfully repaired with a pectoralis major muscle flap through a cervical approach.

Case presentation

A 66-year-old woman with esophageal cancer underwent transthoracic esophagectomy with three-field lymph node dissection via a muscle-sparing thoracotomy as previously reported [3], with gastric conduit reconstruction and an intrathoracic anastomosis. A high-dose proton pump inhibitor (PPI) was administered postoperatively due to the patient's history of gastric ulcers; she discontinued the medication of her own volition.

Three years after surgery, she was admitted to a local hospital for mediastinitis due to a perforated gastric ulcer in the conduit (Fig. 1a). She was treated with antibiotics and fasting. Seventeen days later, she had hematemesis and was diagnosed with a gastro-aortic fistula due to a gastric ulcer (Fig. 1b, c). She was transferred to a nearby university hospital with shock status and underwent endovascular aortic repair urgently, using two GORE® TAG® devices (W.L. Gore & Associates, Flagstaff, AZ). Two days later, total resection of the gastric tube was performed via a right posterolateral thoracotomy. There was an abscess cavity between the gastric tube and the descending aorta which consisted of necrotic tissue and old blood. A 2-cm wall defect was found on the right wall of the middle of gastric tube. The clot-filled gastric tube was resected. The perforation of the descending aorta was left. During this operation, a tracheal injury occurred while the remnant esophagus was being separated from the trachea; this injury was subsequently repaired by patching the stump of the esophagus to the injury site. Tracheostomy and a feeding jejunostomy were also performed. The operative time was 8 h and 40 min, and the blood loss was 2380 ml. The remnant esophagus had been decompressed by nasal tube since the total resection of gastric conduit till the following reconstructive surgery. Two months later, a descending aortic replacement was performed due to infection of the stent graft. Stent graft was removed, and the descending aorta between the fifth vertebra and the eleventh vertebra level was replaced with rifampicin-soaked 24-mm J graft (JUNKEN MEDICAL, Tokyo, Japan). Infected vascular intima of the aorta around the gastro-aortic fistula was resected. The operative time was 8 h and 10 min. Purulent matter was found around the stent graft, and *Candida albicans* was recognized by the bacterial culture of the pus. Postoperative severe pneumonia due to methicillin-resistant *Staphylococcus aureus* (MRSA) occurred after aortic replacement and required artificial respirator. Postoperative pneumonia was gradually improved by antibiotics. Three months later, she was transferred to previous local hospital. When a TEF developed 6 months after the first operation, in spite of decompression of the remnant esophagus by nasal tube, she still had required respirator due to prolonged postoperative pneumonia. Her poor general condition could not allow reconstructive surgery. She could withdraw from respirator 5 months after the aortic replacement (7 months after the first operation). Though she suffered from repeated bouts of aspiration pneumonia, she could walk after rehabilitation for 5 months (1 year after the first operation), and transferred to our hospital for reconstructive surgery. This patient's time course is summarized in Fig. 2.

Bronchoscopy showed a fistula on the membranous portion of the trachea (Fig. 3a). Gastrointestinal endoscopy revealed a fistula in the stump of the esophagus (Fig. 3b). Computed tomography showed the TEF to be on the cervicothoracic border (Fig. 3c). The fistula was formed between the trachea and the esophageal stump on the cervicothoracic border (Fig. 3d). The cervical esophagus was accessed through a cervical approach, and the fistula was ligated and divided (Fig. 4a, b). A pectoralis major muscle flap was used to cover the defect and lay under the trachea (Fig. 4c, e). Esophageal reconstruction using the pedunculated jejunum with a microvascular anastomosis was performed via a subcutaneous route (Fig. 4d, e). The total operative time was 8 h and 54 min. Intraoperative blood loss was 453 ml. The postoperative course was uneventful. She was transferred to the previous hospital on postoperative day 14 and was discharged after 6 months of physical and dysphagia rehabilitation.

Discussion

In patients with TEF after esophagectomy, the latissimus dorsi muscle is the easiest muscle from which to fashion a flap for coverage, but it is often not usable as it is transected in a posterolateral thoracotomy. Though various repair techniques have been reported, the choice of which muscle to use for the repair depends on the location of the fistula. A pedicled posterior pericardial flap or diaphragmatic flap is useful for a fistula located near the carina or near a peripheral bronchus [4, 5]. A pectoralis major muscle flap or sternocleidomastoid muscle flap is useful for a fistula near or in the neck [6, 7]. The intercostal muscle flap can usually reach the whole intrathoracic trachea and bronchus and is a highly versatile option [8].

In this patient, there were several complicating factors including the surgical approach to the TEF given dense adhesions with two prior thoracotomies, flap choice, and conduit choice for esophageal reconstruction. Fortunately, the TEF was located on the cervicothoracic border, and a cervical approach was therefore chosen. A pectoralis major muscle or sternocleidomastoid muscle (SCM) flap can be suitable for repairing this tracheoesophageal fistula. A pectoralis major muscle flap is larger and thicker, and its covering area is wider. A SCM flap can be created easier in the same operative field. The larger pectoralis major muscle flap is considered to be more suitable for this patient to fill the dead space behind the membranous portion of the trachea. There was a problem about blood supply of SCM in this case. The upper third of SCM is supplied by branches of occipital artery. The middle third of SCM is supplied by branches of superior thyroid artery. The lower third of SCM is supplied by branches of the suprascapular artery [9]. There are two types of SCM flap: the superiorly based flap which is the commonly used and supplied from occipital artery and superior thyroid artery and the inferiorly based flap which is suitable for the lesion on the lower neck or upper mediastinum [10]. Though the inferiorly based sternocleidomastoid muscle flap was required according to the fistula position, the necrosis of the flap might occur because of no blood supply from branches of superior thyroid artery and suprascapular artery by previous cervical lymph node dissection. Therefore, the pectoralis major muscle was chosen over the SCM. With respect to esophageal reconstruction, small intestine reconstruction using the pedunculated jejunum with a microvascular anastomosis was chosen over a colonic conduit as there were dense adhesions of the transverse colon to the upper abdominal organs due to a previous total resection of the former gastric conduit.

During gastric conduit resection, dense adhesions around the conduit, particularly around the esophagogastrostomy in the upper mediastinum [11], make dissection difficult and a tracheobronchial injury a possibility. In this case, a tracheal injury occurred while the remnant esophagus was being dissected from the trachea via a thoracotomy. The injury was repaired with the remnant esophagus patch and resulted in a delayed TEF. Because the patient had previously undergone a muscle-sparing thoracotomy for esophageal cancer, thus preserving the latissimus dorsi muscle, a posterolateral thoracotomy with a latissimus dorsi muscle flap or intercostal muscle flap would have been a good option for repair of the initial tracheobronchial injury. When the tracheal injury occurred, the surgeons should have created an intercostal muscle flap to repair the injury and then performed a cervical esophagostomy. A pectoralis major muscle flap or a sternocleidomastoid muscle flap could also have been an option as the injury was near the neck.

The primary cause of this gastro-aortic fistula was discontinuation of PPI medication of her own volition. The frequency of peptic ulcer in the reconstructed gastric tube was reported to be 6.6–19.4% [12–15]. The mortality of patients with perforation of gastric tube ulcer was 56.5% in the review of Japanese literature and 84.6% in the review of the English literature [16]. Once gastric tube ulcer develops to gastro-aortic fistula, it causes a fatal result. We recommend PPI medication for patients with gastric tube reconstruction after esophagectomy.

Fig. 1 a Gastrointestinal endoscopy showed an ulcerated lesion on the right wall of middle of gastric tube. b Horizontal and c sagittal enhanced computed tomography image showed an irregular ulceration on the anterior wall of the descending aorta, no extravasation, and absence of the descending aortic wall and gastric wall, suggesting sealed rupture of the descending aorta (yellow arrow)

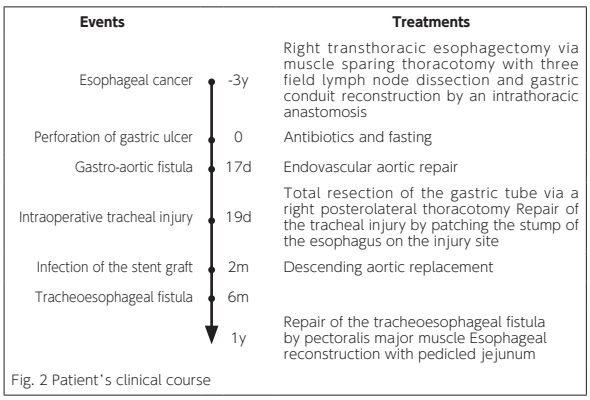

Fig. 2 Patient's clinical course

Fig. 3 a Bronchoscopy showed the fistula on the membranous portion of trachea; a bubble arose from the fistula (white arrow). b Gastrointestinal endoscopy revealed a pinhole in the stump of the esophagus and the staple line (white arrow). c Sagittal computed tomography image showing the tracheoesophageal

fistula on the cervicothoracic border (white arrow). d Schema of the tracheoesophageal fistula
Fig. 4 a Cervical incision line. b The cervical esophagus was accessed through a cervical approach, and the fistula was ligated (white arrow). c A pectoralis major muscle flap was fixed to the fistula site, underneath the trachea. Pectoralis major muscle flap under the trachea (white arrow). d Esophageal reconstruction using the pedunculated jejunum with a microvascular anastomosis was performed via a subcutaneous route. e A schema of the operation

Conclusions

A TEF located near the cervicothoracic border was successfully treated with a pectoralis major muscle flap through a cervical approach. Because total resection of a gastric conduit in the posterior mediastinum carries a risk of tracheobronchial injury, thoracotomy with creation of an intercostal muscle flap should be performed in preparation for a tracheobronchial injury in such situations. If such an injury occurs, surgeons should be able to repair the injury using a suitable flap depending on the injury site.

Abbreviations

PPI: Proton pump inhibitor; SCM: Sternocleidomastoid muscle; TEF: Tracheoesophageal fistula

Authors' contributions

MF, YS, HF, KI, and YK performed the surgery. YS and HF took charge of postoperative care in our hospital. AH took charge of conservative therapy for mediastinitis due to a perforated gastric ulcer in the conduit and postoperative physical and dysphagia rehabilitation in the local hospital. YS prepared the manuscript. MF and MN assisted in drafting the manuscript and reviewed the article. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This study was carried out in accordance with the principles of the Declaration of Helsinki.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Competing interests

The authors declare that they have no competing interests.

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Clinical value of a prophylactic minitracheostomy after esophagectomy : analysis in patients at high risk for postoperative pulmonary complications

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Abstract

Background : The aim of this study is to evaluate the clinical value of a prophylactic minitracheostomy (PMT) in patients undergoing an esophagectomy for esophageal cancer and to clarify the indications for a PMT.
Methods : Ninety-four patients who underwent right transthoracic esophagectomy for esophageal cancer between January 2009 and December 2013 were studied. Short surgical outcomes were retrospectively compared between 30 patients at high risk for postoperative pulmonary complications who underwent a PMT (PMT group) and 64 patients at standard risk without a PMT (non-PMT group) . Furthermore, 12 patients who required a delayed minitracheostomy (DMT) due to postoperative sputum retention were reviewed in detail, and risk factors related to a DMT were

also analyzed to assess the indications for a PMT.
Results : Preoperative pulmonary function was lower in the PMT group than in the non-PMT group : FEV1.0 (2.41 vs. 2.68 L, p = 0.035), and the proportion of patients with FEV1.0% <60 (13.3% vs. 0%, p = 0.009). No between-group differences were observed in the proportion of patients who suffered from postoperative pneumonia, atelectasis, or re-intubation due to respiratory failure. Of the 12 patients with a DMT, 11 developed postoperative pneumonia, and three required re-intubation due to severe pneumonia. Multivariate analysis revealed FEV1.0% <70% and vocal cord palsy were independent risk factors related to a DMT.
Conclusion : A PMT for high-risk patients may prevent an increase in the incidence of postoperative pneumonia and reintubation. The PMT indications should be expanded for patients with vocal cord palsy or mild obstructive respiratory disturbances.
Keywords : Minitracheostomy, Postoperative pneumonia, Esophagectomy

Background

In Japan, the standard surgical procedure for esophageal cancer is subtotal esophagectomy with extended lymph node dissection, which requires the skeletonization of the upper mediastinal structures. This procedure is highly invasive, with high morbidity and mortality rates [1, 2]. Postoperative pneumonia is the most serious complication after esophagectomy and is a major risk factor for inhospital mortality [3]. Impairment of the swallowing function due to cervical lymph node dissection and vocal cord palsy resulting from para-laryngeal nerve lymph node dissection both cause pulmonary aspiration. The impairment of postoperative pulmonary function and postoperative chest pain induce difficulty in expectoration, which can lead to sputum retention and postoperative pneumonia.
Although bronchoscopic aspiration is typically performed for sputum retention, this procedure requires trained bronchoscopists; a significant delay often occurs from onset to treatment. Bronchoscopic aspiration places a large burden on patients. Local anesthetic administered to the mucous membranes of the pharynx, larynx, and trachea often induces the pulmonary aspiration of intraoral bacteria. However, a minitracheostomy allows nursing staff without specialized training to have immediate access to the bronchial tree. The introduction of a catheter into the trachea through the minitracheostomy typically evokes an effective cough that helps clear secretions.
Previous authors have reported that a prophylactic minitracheostomy (PMT) helps prevent postoperative pulmonary complications in patients who undergo pulmonary resection for lung cancer [4–8]. However, given the limited number of available reports, the clinical value of a PMT is unclear in patients undergoing an esophagectomy. Since January 2009, we have used a PMT in patients at a high risk for postoperative pulmonary complications to decrease these complications. The aim of this study was to evaluate the clinical value of a PMT in patients undergoing an esophagectomy for esophageal cancer and to clarify the indications for a PMT.

Methods

Patients

From January 2009 to December 2013, 99 patients underwent a right transthoracic esophagectomy via muscle sparing thoracotomy (MST) as reported previously [9]. Of these, two patients with a previous laryngectomy and one patient with a synchronous laryngectomy were excluded. Two other patients who underwent a tracheostomy for delayed extubation were also excluded. Thus, the remaining 94 patients were subjected to analysis. The ethical committee of Nagoya University Hospital approved our study (No. 2016-0361); written informed consent was obtained from all patients.

Surgical procedures

All patients underwent a right transthoracic esophagectomy via MST with mediastinal lymphadenectomy, including bilateral recurrent laryngeal nerve lymph node dissection and laparotomy for dissecting abdominal lymph nodes, to establish a reconstructive conduit. Thoracotomy was followed by laparotomy in patients with borderline resectable tumors, while laparotomy was followed by thoracotomy in all other patients. The gastric tube was selected as the primary reconstructive conduit. The percutaneous route was chosen in patients who were older or who had liver cirrhosis, and the retrosternal route was used in patients with possible residual tumors (R1/2 resection). In the other patients, the choice of the reconstruction route that was used depended on the surgeon's preference. Reconstruction with a pedicled jejunum was performed via the percutaneous route in all patients who had previously undergone or synchronously underwent gastrectomy.

Prophylactic minitracheostomy

The tracheal tube was routinely extubated on the first postoperative day if the general condition of the patients was stable. The degree of vocal cord palsy was evaluated by bronchoscopy in all patients just after extubation, and a PMT was subsequently performed using a Minitrach II® (SIMS Portex, Hythe, Kent, UK) with the percutaneous Seldinger technique for patients at high risk of postoperative pulmonary complications. These patients included elderly patients over 80 years of age, patients with vocal cord palsy and the presence of a slit between the vocal cords, patients with low pulmonary function [(a forced expiratory volume in 1 s (FEV1.0) <1.5 L or a percent predicted forced expiratory volume in 1 s (FEV1.0%) <60%)], patients with preoperative pneumonia, including interstitial pneumonia, and patients with aspiration noted in an upper gastrointestinal image (Table 1). Routine prophylactic aspiration by bronchoscopy was never performed. A mini-tracheal tube was extubated unless the patients developed pulmonary aspiration after the start of oral intake. A total of 30 patients underwent a PMT; 16 patients were selected to undergo a PMT before surgery, and the remaining 14 patients underwent a PMT after surgery. We performed a delayed minitracheostomy (DMT) following bronchoscopic aspiration for patients with postoperative sputum retention despite the presence of vocal cord palsy.

Perioperative care

All patients received intravenous injections of methylprednisolone to attenuate the inflammatory responses as follows : 250 mg intravenously 1 h before the start of surgery, 125 mg on day 1, and 80 mg on day 2. One epidural catheter was intubated between the fifth and sixth thoracic vertebra, and another epidural catheter was intubated between the ninth and tenth thoracic vertebra. Continuous epidural anesthesia with fentanyl and ropivacaine or levobupivacaine was used until day 6. An intravenous drip injection of pentazocine (15 mg) or buprenorphine (3 mg) was administered as needed until day 10. An injection of loxoprofen or pregabalin was administered via feeding tube from day 11 until the start of oral intake. Computed tomography (CT) was performed on day 7 in all patients. Atelectasis was assessed by radiological evidence of plate atelectasis, labor collapse, or total lung collapse as shown on the CT image.
Postoperative complications were defined as any event requiring specific medical or surgical treatment and were assessed according to the Clavien-Dindo classification [10]. A PMT was not considered to be a grade 3 pulmonary complication.

Table 1 Indication of prophylactic minitracheostomy

Indication	Number of patients
Preoperative	
Old age	2
Low pulmonary function	5
Preoperative pneumonia	5
Aspiration	3
Low pulmonary function + Aspiration	1
Postoperative	
Vocal cord palsy	14

Statistical analyses

The results are expressed as the median (range). Fisher's exact probability test and the Mann-Whitney U test were used for analysis as appropriate. Univariate and multivariate analyses were performed using a logistic regression model to identify the independent factors that were associated with postoperative pneumonia. In the multivariate analysis, the factors that showed a p value of <0.200 in the univariate analysis were selected and subjected to a stepwise logistic regression analysis. All statistical analyses were performed with SPSS software version 20.0 J. The two-sided p values were calculated and are presented. A p value of <0.05 was considered statistically significant.

Results

Patient characteristics

No significant differences were observed between the PMT and non-PMT groups in terms of the age, gender, tumor location, clinical stage, or proportion of patients who underwent preoperative chemotherapy, preoperative chemoradiotherapy, or a salvage operation (Table 2). Regarding the preoperative pulmonary function, the FEV1.0 was significantly lower in the PMT group than that in the non-PMT group. The proportion of patients with FEV1.0% less than 60% was significantly higher in the PMT group than that in the non-PMT group.

Table 2 Patients' characteristics

Variables	PMT group (n = 30)	Non-PMT group (n = 64)	P
Age [year]	68.5 (51-86)	65.0 (43-78)	0.071
Gender (male/female)	23/7	57/7	0.131
Location of tumor, n (%)			0.413
Ut	6 (20.0)	6 (9.4)	
Mt	13 (43.3)	36 (56.2)	
Lt	9 (30.3)	16 (25.0)	
Ae	2 (6.7)	6 (9.4)	
cStage (UICC 7th), n (%)			0.153
I	5 (16.7)	25 (39.1)	
II	10 (33.3)	14 (21.9)	
III	12 (40.0)	20 (31.2)	
IV	3 (10.0)	5 (7.8)	
Neoadjuvant chemotherapy, n (%)	14 (46.7)	26 (40.6)	0.652
Neoadjuvant chemoradiotherapy, n (%)	6 (20.0)	5 (7.8)	0.099
Salvage operation, n (%)	1 (3.3)	4 (6.3)	1.000
Preoperative pulmonary function			
VC [L]	3.51 (2.03-5.43)	3.66 (2.05-5.57)	0.113
%VC	114 (67-134)	110 (76-166)	0.703
FEV1.0 [L]	2.41 (1.11-3.36)	2.68 (1.59-4.13)	0.035
FEV1.0%	71.5 (53.2-91.3)	76.4 (60.2-93.8)	0.160
FEV1.0% < 60%, n (%)	4 (13.3)	0	0.009

PMT prophylactic minitracheostomy

Surgical procedures

The surgical procedures are summarized in Table 3. No between-group differences were observed in the proportion of patients requiring cervical lymph node dissection, a reconstructive organ, a reconstructive route, and an anastomotic portion. The operative time and blood loss were similar between the two groups.

Postoperative outcomes

The duration of intubation was significantly longer in the PMT group than in the non-PMT group (Table 4). No significant differences were observed between the two groups in terms of the incidence of grade 2 postoperative pneumonia and atelectasis. Of the 64 non-PMT patients, 12 patients required a DMT due to postoperative sputum retention, and seven required re-intubation. The incidence of vocal cord palsy was significantly higher in the PMT group than that in the non-PMT group because a PMT was performed for patients with vocal cord palsy and the presence of a slit between the vocal cords. No between-group differences were observed in terms of paroxysmal tachycardia or anastomotic leakage. The lengths of postoperative hospital stays were not different. One patient died of severe pneumonia on day 34 in the non-PMT group.

Regarding patients with vocal cord palsy, in two patients who underwent the resection of unilateral recurrent nerve involved in metastatic lymph node, ansa cervicalis-recurrent nerve anastomosis was performed simultaneously. Though the vocal palsy was permanent, they kept relatively good phonating function and swallowing function without aspiration. All the other patients with vocal code palsy recovered conservatively within 6 months after the operation. All patients with postoperative aspiration became orally ingestible by swallowing rehabilitation.

Next, we reviewed in detail the 12 patients who underwent a DMT (Table 5). Of these patients, seven had mild obstructive respiratory disturbances, and five had vocal cord palsy. Co-morbidities with liver cirrhosis, heart failure, failed smoking cessation, and walking difficulty were also found.

Table 3 Surgical procedures

Variables	PMT group (n = 30)	Non-PMT group (n = 64)	P
Cervical lymph node dissection, n (%)	24 (80.0)	52 (81.3)	1.000
Reconstructed organ, n (%)			0.064
Stomach	27 (90.0)	46 (71.9)	
Jejunum	3 (10.0)	18 (28.1)	
Reconstructive route, n (%)			0.229
Percutaneous	7 (23.4)	20 (31.2)	
Retrosternal	10 (33.3)	11 (17.2)	
Postmediastinal	13 (43.3)	33 (51.6)	
Anastomotic portion			
Cervical / Intrathoracic	23 / 7	40 / 24	0.240
Operative time [min]	540 (406-732)	584 (306-975)	0.084
Blood loss [ml]	1057 (262-2567)	964 (269-6698)	0.320
Blood transfusion, n (%)	19 (63.3)	33 (51.6)	0.374

PMT prophylactic minitracheostomy

When the 12 patients with a DMT were compared with the 52 patients without a DMT, significant between-group differences were observed in terms of the following parameters : the incidence of postoperative pneumonia (11/12 vs. 14/42, $p < 0.001$, atelectasis (9/12 vs. 11/52, $p < 0.001$), and postoperative hospital stay [50 (18-137) vs. 24 (14-224) days, $p = 0.008$].

Of the 12 patients who received a DMT, three required re-intubation due to severe pneumonia. However, of the 52 patients without a DMT, four underwent re-intubation. These four patients did not undergo a minitracheostomy before re-intubation due to sudden respiratory failure or acute progressive severe pneumonia.

Logistic regression analysis of the risk factors related to DMT

The risk factors related to a DMT were analyzed using univariate and multivariate logistic regression analyses in the 64 non-PMT patients (Table 6). Nine possible risk factors were included in the analysis. The dysfunction of other organs was defined as a history of ischemic heart disease or heart failure, cerebrovascular disease, liver cirrhosis (indocyanine green retention time at 15 min >15%), or renal failure (serum creatinine level > 1.5 mg/ dl). Among these potential risk factors, multivariate analysis identified FEV1.0% < 70% and vocal cord palsy as independent risk factors.

Discussion

Our results demonstrated that the incidence of postoperative pulmonary complications in high-risk patients (the PMT group) was at least equivalent to that in the standard-risk patients (the non-PMT group). A noteworthy observation was that no patient required reintubation in the PMT group. A PMT may prevent an increase in the incidence of postoperative pneumonia and re-intubation in patients at high risk for pulmonary complications. Although no complications related to a PMT were reported in this study, severe complications associated with a minitracheostomy have been reported, such as membranous tracheal injury, bleeding from the anterior cervical vein, hoarseness, and obstructive subglottic granuloma after removal of a minitracheostomy tube [11-13]. A minitracheostomy may prevent elevation of the larynx during swallowing and impair the swallowing function. Therefore, a PMT should be restricted to highrisk patients, and it is important to appropriately select patients requiring a PMT.

Table 4 Postoperative outcomes

Variables	PMT group (n = 30)	Non-PMT group (n = 64)	P
Extubation of tracheal tube [POD]	2 (1-6)	1 (1-11)	0.002
Pulmonary complications, n (%)			
Postoperative pneumonia (≧ CD2)	8 (26.7)	25 (39.1)	0.258
Atelectasis[a]	10 (33.3)	26 (40.6)	0.495
Re-intubation	0	7 (10.9)	0.093
Other complications, n (%)			
Vocal cord palsy	16 (53.3)	12 (18.8)	0.001
Paroxysmal tachycardia	7 (23.3)	13 (20.3)	0.790
Anastomotic leakage	0	8 (12.5)	0.052
Any complication (≧ CD3a), n (%)	5 (16.7)	21 (32.8)	0.137
90-day mortality, n (%)	0	1 (1.6)	1.000
Postoperative hospital day [days]	28 (16-97)	30 (14-226)	0.460

PMT prophylactic minitracheostomy, *CD* Clavien-Dindo classification
[a]diagnosed by computed tomography

Table 5 The characteristics of the patients with delayed minitracheostomy

	Age	FEV1.0% < 70	Vocal cord palsy	Others factors
1	60-69			Failure to cease tobacco
2	60-69	○	○	
3	60-69	○		Liver cirrhosis (ICGR15 = 19%)
4	60-69		○	
5	70-79	○		Walking difficulty
6	70-79			Heart failure (EF48%)
7	40-49			Failure to control pain
8	70-79	○	○	
9	70-79	○		
10	60-69		○	Liver cirrhosis (ICGR15 = 25%)
11	60-69	○		
12	70-79	○	○	

ICGR15 indocyanine green retention time 15 min, *EF* ejection fraction

Table 6 Uni-and multivariate analyses for risk factors related to delayed mini-tracheostomy

Variables		DMT	Univariate	Multivariate	
	n	n (%)	*P*	HR (95%-CI)	*P*
Age			0.238		
75>	55	9 (16.4)			
≧75	9	3 (33.3)			
Brinkman Index			0.968		
800>	37	7 (18.9)			
≧800	27	5 (18.5)			
FEV1.0%			0.061		0.032
≧70	42	5 (11.9)		1	
< 70	22	7 (31.8)		5.06 (1.15–22.21)	
Clinical stage (UICC 7th)			0.838		
I	25	5 (20.0)			
II III IV	39	7 (17.9)			
Preoperative chemoradiotherapy			0.533		
Absent	55	11 (20.0)			
Present	9	1 (11.1)			
Cervical lymph node dissection			0.162		
Absent	12	4 (33.3)			
Present	52	8 (15.4)			
Reconstructive organs			0.790		
Stomach	46	9 (19.6)			
Jejunum	18	3 (16.7)			
Vocal cord palsy			0.032		0.017
Absent	52	7 (13.5)		1	
Present	12	5 (41.7)		6.90 (1.41–33.85)	
Dysfunction of other organs			0.073		
Absent	54	8 (14.8)			
Present	10	4 (40.0)			

DMT delayed mini-tracheostomy, *HR* hazard ratio, *CI* confidence interval

Regarding our PMT indications in this study, age, low pulmonary function, and vocal cord palsy were reported to be associated with postoperative pneumonia after esophagectomy [14, 15]. Aspiration of oral bacteria is commonly known to cause postoperative pneumonia [16]. Vocal cord palsy with a slit and reduced swallowing function with aspiration on the upper gastrointestinal image were therefore included as indications for a PMT. In patients with preoperative pneumonia including interstitial pneumonia, worsening of this condition due to an esophagectomy can be lethal; thus, preoperative pneumonia was also included as an indication for PMT.

A routine tracheostomy may be safer than a minitracheostomy when emergency airway management is needed. However, a tracheostomy leads to temporary voicelessness, which is stressful for patients and causes impairment of the swallowing function due to the restriction of the elevation movement of the larynx during swallowing. Moreover, a tracheostomy can occasionally cause severe complications such as recurrent laryngeal nerve injury, tracheoesophageal fistula, or tracheo-brachiocephalic artery fistula. We propose that a prophylactic tracheostomy is too invasive.

In this study, none of the 30 patients who received a PMT according to our indications required re-intubation, whereas 12 of the non-PMT patients required a DMT due to postoperative sputum retention, and three developed severe pneumonia and required re-intubation. A multivariate analysis revealed that FEV1.0% <70% and vocal cord palsy were independent risk factors related to a DMT. Therefore, the indications for a PMT should be expanded for such patients despite the presence of a slit between the vocal cords. After this analysis, we expanded the indications for a PMT.

Although we focused on pulmonary function and aspiration to define the indications for a PMT, the DMT group included patients with health problems other than pulmonary function, such as liver cirrhosis, heart failure, and walking difficulty. In the prospective randomized trial reported by Pramod et al. [6, 17], the indications for a PMT included ischemic heart disease and cerebrovascular disease, which are likely to be exacerbated by postoperative hypoxia. In their study, some patients developed acute myocardial infarction or cerebellar infarction secondary to sputum retention. In addition to pulmonary function and aspiration, other organ disorders, such as heart failure, ischemic heart disease, liver cirrhosis, cerebrovascular disease, and performance status should be considered for a PMT.

In the present study, 11 of the 12 patients with a DMT due to postoperative sputum retention developed postoperative pneumonia, and three patients progressed to severe pneumonia. These observations demonstrate that a DMT after postoperative sputum retention cannot prevent postoperative pneumonia. In patients with sputum retention, oral bacteria may have dripped into the bronchial tree gradually due to postoperative vocal cord palsy and an impairment of swallowing function immediately after extubation. Thus, when sputum retention occurs, a pulmonary infection may have already developed. It is therefore important to prophylactically perform a minitracheostomy. Some limitations were associated with this study. First, this is a retrospective study with only a small number of patients. Second, most of our patients underwent cervical lymph node dissection which is not generally performed in western country. Cervical lymph node dissection was reported to increase the incidence of vocal cord palsy [1] and impair swallowing function [18], and may lead to the increase of the incidence of postoperative pneumonia. Therefore, our results do not apply to patients without cervical lymph node dissection, and it may be necessary to reconsider the indications for a PMT for patients without cervical lymph node dissection. Third, all study patients underwent an open thoracotomy.

The incidence of pulmonary complication in open thoracotomy has been reported to be 12.5 to 39.66% [19]. The incidence of postoperative pneumonia in our study was 35.1%, and not particularly high, compared with open thoracotomy groups in the other studies. However, thoracoscopic esophagectomy has recently become popular and has been reported to reduce pulmonary complications compared to open thoracotomy [19–21]. It may be necessary to reconsider the PMT indications also for patients receiving thoracoscopic esophagectomy. Fourth, because this study did not compare two groups with the same condition, no conclusive results can be drawn from this comparison. A prospective randomized study comparing a PMT group and a non-PMT group of patients at high risk for pulmonary complications is needed.

Conclusion

A PMT for patients at high risk for postoperative pulmonary complications may be effective for preventing an increase in the incidence of postoperative pneumonia and re-intubation. The indications for a PMT should be expanded for patients with mild obstructive respiratory disturbances or vocal cord palsy despite the presence of a slit between the vocal cords.

Abbreviations

CT : Computed tomography; DMT : Delayed minitracheostomy; MST : Muscle sparing thoracotomy; PMT : prophylactic minitracheostomy

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Availability of data and materials

The database of this study may provide insight in clinical and personal information about our patients. Therefore, these data cannot be made publically available unless the approval of the ethical committee of our hospital is obtained.

Authors' contributions

MF, KM, KI, and YS performed the surgery, and took charge of postoperative care. MF and MN analyzed these clinical data. YS prepared the manuscript. MF and MN assisted in drafting the manuscript and reviewed the article. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The ethical committee of Nagoya University Hospital approved our study (No. 2016-0361) ; written informed consent was obtained from all patients.

Consent for publication

Not applicable

Competing interests

All authors declare that they have no competing interests.

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Posterior inferior cerebellar artery with an extradural origin from the V_3 segment: higher incidence on the nondominant vertebral artery

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Abstract
OBJECTIVE : The posterior inferior cerebellar artery (PICA) and the vertebral artery (VA) often exhibit anatomical variations at the craniovertebral junction (CVJ). An example of this is the PICA originating extradurally from the V_3 segment of the VA. To date, some cadaveric investigations have been reported, but the incidence and relationship of this variation to the VA and the atlas as observed on clinical imaging have not been discussed. This study evaluated the prevalence of PICAs originating from the V_3 on CT scanning. Other variations of the atlas and VA were also analyzed.
METHODS : CT images from a series of 153 patients who underwent 3D CT angiography (CTA) were analyzed, and variations of the PICA, VA, and atlas were investigated.
RESULTS : A total of 142 patients (284 sides) were analyzed; 11 patients (7.2%) were excluded due to poor image quality. The most common VA variation was the PICA originating from V_3 (9.5% of 284 sides), which was more frequently observed on the nondominant VA than the dominant VA (22.5% vs 6.25%, p = 0.0005). A VA with a PICA end was identified in 4 sides (1.4%), which is the same incidence as observed in the persistent first intersegmental VA (1.4%). VA fenestration was only found in 1 side (0.35%). Regarding the atlas, ponticulus posticus was observed in 24 sides (8.5%). There was no relationship between the incidence of ponticulus posticus and the variations of the VA.
CONCLUSIONS : A PICA originating from V_3 was the most common VA variation at the CVJ and was more common on the nondominant VA. Three-dimensional CTA is useful for the evaluation of this variance. Surgeons should be mindful of this variation during operations.

Effect of Vitreomacular Separation on Macular Thickness Determined by Spectral-domain Optical Coherence Tomography

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Abstract
Purpose : To determine the effects of vitreomacular separation on macular thickness.
Methods : This was a retrospective, observational, cross-sectional study. Average foveal and central minimum thicknesses were measured by spectral-domain optical coherence tomography (SD-OCT) in 308 eyes of 308 healthy subjects (healthy group) and 298 normal fellow eyes of 298 patients with a unilateral macular

hole (MH group). Multiple regression analyses were performed to determine the effects of various factors on the macular thickness.
Results : The mean age of healthy group was 67.3±9.6 years (range, 40-88 years) and that of the MH group was 67.8±7.0 years (range, 43-91). SD-OCT images showed that 149 eyes (48.4%) in healthy group and 174 eyes (58.4%) in MH group had a vitreomacular separation. In the healthy group, the central minimum thickness of eyes with a vitreomacular separation (196 μm) was significantly thinner than those without a vitreomacular separation (205 μm; P<.001). In MH group, the average foveal thickness (234 μm) and the central minimum thickness (177 μm) in eyes with a vitreomacular separation were thinner than those without it (247 μm and 199 μm, respectively; both P<.001). Multiple regression analyses showed that a vitreomacular separation was significantly correlated with a thinner central minimum thicknesses in both groups (P<.001) and also with the average foveal thickness in the MH group (P<.001).
Conclusions : A vitreomacular separation causes thinning of the central fovea in both the healthy eyes and the normal fellow eyes of unilateral MH patients; the extent of foveal thinning is greater in the MH group.

Introduction

During the development of a posterior vitreous detachment (PVD), the vitreous adhesion to the fovea plays a key role in the development of a macular hole (MH) and the vitreomacular traction syndrome [1-6]. The posterior vitreous adhesion to the fovea is divided into two types by the International Vitreomacular Traction Study Group; vitreomacular traction with foveal deformation and a vitreomacular adhesion without foveal deformation [7]. Vitreomacular tractions are found more frequently in the asymptomatic fellow eyes of unilateral MH patients than in the eyes of healthy subjects [8]. Also, an abnormal vitreomacular adhesion appears to precede the development of a MH.

Spectral-domain optical coherence tomography (SD-OCT) allows clinicians to obtain the detailed views of the vitreomacular interface [9-15]. Several studies using time-domain OCT [16-18] and SD-OCT [19-25] on the healthy eyes reported that the macular shape was related to the age and sex of the individual and the axial length of the eye.

Thus, the aim of this study is to characterize the differences in the macular thicknesses based on status of the vitreous attachment in the normal eyes of healthy subjects and the normal fellow eyes of patients with a unilateral MH.

Materials and Methods

This was a multicenter, retrospective, observational, cross-sectional study of the macular thickness of the normal eyes of healthy subjects and the normal fellow eyes of patients with a unilateral MH. The patients were examined intermittently between September 2008 through October 2013 at Shinjo Ophthalmologic Institute, Kami-iida Daiichi General Hospital, Nishigaki Eye Clinic, and Yada Eye Clinic.

The study protocols were approved by the Ethics Committees of each institution, and all of the procedures adhered to the tenets of the Declaration of Helsinki. An informed consent was obtained from the patients to perform the clinical measurements, and permission was obtained from all patients to use the collected data for future research studies.

This study was conducted on the fellow eyes of patients with unilateral cataracts without any retinal diseases (healthy group), and the fellow eyes of patients with unilateral idiopathic MH diagnosed as normal by slit-lamp biomicroscopy (MH group). The exclusion criteria were eyes with the best-corrected visual acuity (BCVA) less than 20/20, presence of significant cataract, prior ocular surgery, refractive error less than - 6.00 diopters (D) and more than +3.00 D, and ocular diseases such as epiretinal membrane, diabetic retinopathy, hypertensive retinopathy, uveitis, and glaucoma that can affect the macular thickness.

All patients underwent comprehensive ophthalmological examinations including measurements of the refractive errors, best-corrected visual acuity (BCVA) with a Landolt chart at 5 m, axial length by IOL Master (Carl Zeiss Meditec Inc, Dublin, California, USA), and the intraocular pressure with a Goldmann applanation tonometer. In addition, all patients were examined by SD-OCT and slit-lamp biomicroscopy with either contact or noncontact lenses under pupil dilation.

The SD-OCT examinations were performed on all eyes with the Cirrus HD OCT (Carl Zeiss Meditec Inc, Dublin, California, USA) to obtain images of the vitreoretinal interface. The scans were performed with the high-definition mode composed of 5 B-scans, 4096 A-scan resolution, 0.25-mm interval between the neighboring B-scans, and 6×6-mm macular cube scans centered on the fovea. Only images with signal intensities of 7 or more obtained by experienced optometrists were used for the analyses.

The vitreoretinal interfaces were classified into the different types using the methods described by the International Vitreomacular Traction Study Group [7]. A vitreomacular separation was considered to be present when the vitreous was detached from the macula regardless of an attachment at the optic nerve head. The eyes with a vitreomacular separation were subdivided into 2 types; those with a foveal deformation with an anatomical distortion of the foveal surface, and those with a normal contour type without foveal surface deformation. In contrast, a vitreomacular adhesion was defined to be present when a posterior vitreous cortex attached to the macula regardless of a vitreous detachment at the perifoveal regions. The eyes with a vitreomacular adhesion were subdivided into 2 types; the vitreomacular traction type with foveal shape distortions due to the traction, and the normal contour type without macular deformations. In addition, the eyes were further divided by the size of vitreous adhesion; focal (<1500 μm) or broad (≥1500 μm) (Figure 1 a-e).

The average macular thicknesses in the subfields within a 6-mm diameter circle centered on the fovea were determined by Cirrus HD OCT as defined by the Early Treatment Diabetic Retinopathy Study. The subfields included nine regions : central foveal region and the superior, temporal, inferior, and nasal quadrants of the inner and outer rings surrounding the central foveal region. In addition, the central minimum thicknesses were manually measured, which were defined as the distance between the vitreoretinal interface and the anterior border of the highly reflective line representing the retinal pigment epithelium.

The statistical differences of the categorical data between each group were evaluated by chi-square tests and the paired numerical data were analyzed by t tests. The age, sex, axial length, and average macular thicknesses were compared by analyses of variance with the Fisher post hoc tests. Univariate and multivariate regression analyses were used to determine the association of the average foveal thickness and the central minimum thickness with the sex, age, axial length, and the presence or absence of a vitreomacular separation. For multiple linear regression analyses, the parameters with suggestive significant associations in the univariate analysis (P <0.10) were included. Statistical analyses of the data were carried out using Statview software version 5.0 (SAS Institute, Inc, Cary, North Carolina, USA). A P <0.05 was accepted as statistically significant.

Results

Table1 shows the baseline characteristics of the 308 eyes of 308 healthy subjects in the healthy group and 298 normal fellow eyes of 298 patients in the MH group. The mean age in the healthy group was 67.3 ± 9.6 years (range : 40-88 years) and 67.8 ± 7.0 years (range : 43-91 years) in the MH group (P >0.05). There were significant differences in the sex distributions and the axial lengths between the two groups (P = 0.006 and P = 0.004, respectively).

A vitreomacular separation was observed in 174 eyes (58.4%) in the MH group and 149 eyes (48.4%) in the healthy group. A foveal deformation was observed in 87 eyes (50.0%) in the vitreomacular separation with a MH group which was significantly higher than 15 eyes (10.1%) in the healthy group with vitreomacular separation (P <.001). In addition, a vitreomacular traction was observed in 36 eyes (29.0%) in the MH group with a vitreomacular adhesion, and it was observed in only 2 eyes (1.3%) in the healthy group with a vitreomacular adhesion (P <.001).

Table 2 shows the macular thicknesses in eyes with vitreomacular adhesion and separation. In the healthy group, the central minimum thickness was significantly thinner in eyes with vitreomacular separation (196 μm) than in eyes with vitreomacular adhesion (205 μm). The mean age was significantly lower in the vitreomacular adhesion group (63.4 years) than in the vitreomacular separation (71.4 years; P <.001). The percentage of women in the vitreomacular adhesion group was significantly lower (48.4%) than in the vitreomacular separation group (61.7%; P = 0.02).

In the MH group, both the average foveal thickness and the central minimum thickness were thinner in the eyes with a vitreomacular separation than in the eyes with vitreomacular adhesion (234 μm versus 247 μm for the average foveal thickness; 177 μm versus 199 μm for the central minimum thickness). The differences in the average foveal thicknesses between the vitreomacular adhesion and the vitreomacular separation groups were larger in the MH group (12.2 μm) than in the healthy group (3.9 μm). Similar findings were observed for the differences of the central minimum thicknesses between vitreomacular adhesion and the vitreomacular separation groups; 22.3 μm in the MH group and 9.1 μm in the healthy group.

Table 3 shows the demographics of the healthy group based on the vitreomacular interface. The age, sex distribution, average foveal thickness, and central minimum thickness were significantly different for each type of vitreomacular interface (P <.001, P = 0.02, P < .001, P <.001, respectively by analysis of variance). When only the eyes with normal contour were compared, the central minimum thicknesses were significantly thinner in eyes with vitreomacular separation compared to eyes with vitreomacular adhesion (199 μm vs. 205 μm, P <0.05). No significant differences were observed in the average inner and outer rings of each group. Table 4 shows the demographics of the MH group based on the vitreomacular interface. When only the eyes with normal contour were compared, the central minimum thicknesses were significantly thinner in eyes with vitreomacular separation compared to eyes with vitreomacular adhesion (184μm vs. 198 μm, P<0.05).

Table 5 shows univariate and multiple regression analyses of all eyes. In the healthy group, the average foveal thickness was significantly affected by the sex (P =0.001) and the axial length (P < .001). The central minimum thickness was significantly correlated with the presence of vitreomacular separation (P < .001).

Table 6 shows univariate and multiple regression analyses in the MH group. The average foveal thickness was significantly affected by the sex (P <.001), the axial length (P = 0.04) and the presence of vitreomacular separation (P <.001). The central minimum thickness was significantly affected by the sex (P =0.002) and the presence of vitreomacular separation (P <.001).

Table 7 and Table 8 show univariate and multiple regression analyses in the healthy group and in the MH group, respectively, using the data only from normal contour eyes. In the healthy group, the central minimum thickness was significantly affected by the presence of vitreomacular separation (P =0.0093). Also, in the MH group, the average foveal thickness and the central minimum thickness were significantly affected by the presence of vitreomacular separation (P =0.025 and P=0.008, respectively)

Discussion

We determined the effects of vitreomacular separation on macular thickness in the healthy subjects and the normal fellow eyes of MH patients. The average foveal and central minimum thicknesses were thinner in eyes with vitreomacular separation than in eyes with vitreomacular adhesion. In contrast, there were no differences in macular thicknesses at the perifoveal region. These results indicated that the significant retinal thinning occurred only at the foveal region after the vitreomacular separation. However, the macular thickness decrease at the fovea appeared to be greater in the fellow eyes of the unilateral MH patients than in the healthy eyes.

Age-related PVDs in healthy eyes develop initially as a localized perifoveal detachment of the posterior hyaloid membrane with a persistent adhesion to the fovea and optic nerve head [4-6]. The detachment slowly expands and eventually results in a vitreomacular separation but the vitreopapillary adhesion remains. After the vitreous separation from the fovea, operculum-like structures are often seen in the detached hyaloid membrane with a deformation of the foveal surface in the OCT images (Figure 1 f). Two distinct types of opercula have been reported in eyes with stage 3 MH; a pseudo-opercula containing only glial tissue, and a true opercula containing both glial and foveal neural tissues [26]. Although it is not certain whether an operculum-like structure in healthy eyes with a vitreomacular separation and in stage 3 MH eyes are the same, it is possible that an avulsion of foveal tissue might have occurred during the development of the vitreomacular separation in the healthy eyes resulting in the foveal thinning and deformation [3, 11-12].

We reported in an earlier study that the incidences of superficial foveal deformation associated with vitreomacular traction and vitreomacular separation were higher in the normal fellow eyes of unilateral MH patients than in the eyes of healthy subjects [8]. Similar results were obtained in this study; the incidences of vitreomacular traction and foveal deformation were significantly higher in MH group (29% and 50%, respectively) than in healthy group (1% and 10%, respectively). Also, the incidence of focal vitreomacular adhesion (<1500 μm) was higher in MH group than in healthy group (49% versus 15%). These results suggest that the eyes of unilateral MH patients have stronger vitreofoveal adhesion than the eyes of healthy subjects.

The foveal thinning after vitreomacular separation may be related to the arrangement of the Müller cell processes which make up most of the inner third of the foveolar center, termed as the Müller cell cone [27]. The most common appearance of a MH is a horizontal foveal split resulting in a pseudocyst [1-3]. An unroofing of a foveal pseudocyst cause a lamellar hole if the base of the pseudocyst is preserved. A full-thickness MH will develop if the outer retinal layer is disrupted during the process of a horizontal foveal split. Gass suggested that an avulsion of the Müller cell cone can lead to a full-thickness MH [27]. The physiological process of the development of a vitreomacular separation could remove the superficial part of the Müller cell cone.

A decrease in the central minimum thickness after vitreomacular separation was also found in eyes with normal foveal contour in both the healthy and the MH groups. Thus, there appears to be some mechanism by which an avulsion of foveal tissue causes foveal thinning. A possible mechanism for this is the release of traction exerted by the adhesion of posterior hyaloid membrane [28]. In addition, Ooto et al suggested that a subclinical vitreous traction may cause foveal thickening [20].

Another possible reason for the decrease of average foveal and central minimum thicknesses after vitreomacular separation may be the age-related macular thinning because the average age of patients with a vitreomacular separation was significantly higher than those without a vitreomacular separation. Previous SD-OCT studies showed that the macular thickness was significantly correlated with age, sex, and axial length with regional variations [20-21, 23]. Histological studies of human retinas have demonstrated a decrease in density of photoreceptors and retinal ganglion cells in older individuals [29-30]. However, several studies have found that the central minimum thickness was not correlated with age, although the foveal and the inner and outer ring thicknesses decreased as the mean age increased [20-21]. In this study, multiple regression analyses showed no significant correlation between the age and the average foveal and central minimum thicknesses suggesting that involvement of the age-related macular thickness changes were not significant factors influencing the decrease of the foveal thickness after a vitreomacular separation.

Although the strengths of this study include the large sample size and the use of SD-OCT, our study had several limitations. First, this was a retrospective clinic-based study in which selection bias was inherent. Second, because of the cross sectional nature of this study, the data did not provide definite information about a cause-and-effect relationships between the macular thickness and the factors studied. Third, evaluations of the SD-OCT findings and the measurement of central minimum thickness were subjective. Finally, only Japanese patients were studied, so the results may be different in other ethnic population.

In conclusion, a vitreomacular separation is associated with a thinning of the fovea in both healthy eyes and the normal fellow eyes of patients with a unilateral MH. In addition, the effects of a vitreomacular separation on the foveal thicknesses were greater in the normal fellow eyes of unilateral MH patients than in the healthy subjects. Further longitudinal studies are needed to confirm the effects of a vitreomacular separation on the macular thickness.

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Decrease of the Foveal Avascular Zone Area after Internal Limiting Membrane Peeling : Single Case Study

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Abstract

Purpose :

To report a patient whose foveal avascular zone (FAZ) decreased after vitrectomy with internal limiting membrane (ILM) peeling.

Methods :

A 58-year-old woman underwent successful phacovitrectomy with ILM peeling for a thin epiretinal membrane in an eye with a normal foveal contour. Optical coherence tomography angiographic *en face* images of the 3 mm x 3 mm superficial and deep inner retinal vascular plexuses were examined preoperatively, and on days 1, 2, 9, and 37 postoperatively. The changes in the FAZ areas and the thicknesses of the parafoveal retinal layers at 0.5 mm from the foveal center were assessed in the vertical and horizontal B-scan images.

Results :

The areas of the superficial and deep FAZ decreased after the surgery. The course of the postoperative decrease of the FAZ area in the superficial plexus can be fit by a hyperbolic curve (R^2=0.993). An increase in the thicknesses of the retinal nerve fiber layer, ganglion cell-inner plexiform layer, and inner nuclear layer was observed at all times postoperatively.

Conclusions :

We observed one case that the FAZ area decreased and the parafoveal inner retinal thickness increased after the vitrectomy with ILM peeling. The decrease in the FAZ area suggests that a centripetal movement of the inner retinal layer is probably due to the ILM peeling.

Introduction

The foveal avascular zone (FAZ) is a capillary-free area bordered by the foveal capillaries running in the inner retinal layers. Optical coherence tomography angiography (OCTA) was recently introduced as a noninvasive method that can obtain *en face* images of both the superficial and deep capillary plexuses.[1]

The size of the FAZ area is correlated with the sex,[2] age,[2-6] and foveal thickness.[5-6,7-11] However, the effect of internal limiting membrane (ILM) peeling on the FAZ area has not been well determined. Thus, the purpose of this study was to determine the effect of vitrectomy with ILM peeling on the size of the FAZ. To accomplish this, we performed vitrectomy with ILM peeling on an eye with a thin epiretinal membrane (ERM) and a normal foveal contour. The OCTA *en face* images of the superficial and deep retinal vascular plexuses were examined preoperatively, and at

days 1, 2, 9, and 37 postoperatively.

Case Report

A 58-year-old woman presented with a slight decrease in vision in her right eye (20/25) of 1 year duration. Ophthalmoscopy showed that she had a thin ERM over the fovea. The patient underwent phacoemulsification, intraocular lens implantation followed by vitrectomy, ERM peeling, and brilliant blue G-assisted ILM peeling within the vascular arcade. After the surgery, her visual acuity improved to 20/20 at day 37 postoperatively. A patient did not have systemic risk factors such as diabetes mellitus or uncontrolled hypertension that could affect the retinal morphology. Also, she did not have ocular diseases such as myopia, glaucoma, age-related macular degeneration that could affect retinal morphology except for a thin ERM.

A written informed consent was obtained from a patient to collect data and to use accompanying images and data for future research study with the care not to publicize patient's name and initial anywhere.

The sequential changes of the foveal morphology were determined by swept-source optical coherence tomography (SS-OCT) with the DRI OCT-1 instrument (Topcon, Atlantis, Tokyo, Japan). The scans were performed with the angioretina mode to obtain 3 mm x 3 mm *en face* images of the superficial and deep vascular plexuses. The retinal surface maps were reconstructed from the 3-dimensional cube scans. The FAZ area was measured by manual delineation with the ImageJ software (National Institutes of Health, ImageJ, Bethesda, MD, USA) .

The vertical and horizontal B-scan images through the foveal center were analyzed to determine the thicknesses of the retinal nerve fiber layer (RNFL), ganglion cell-inner plexiform layer (GCIPL), inner nuclear layer (INL), outer plexiform layer (OPL), and outer nuclear layer (ONL). Manual measurements were made of the horizontal and vertical lines at 0.5 mm from the foveal center.

The sequential retinal surface maps and the OCTA images showing the FAZ in the superficial and deep plexuses at each time are shown in Figure 1. The surface maps showed an increase of the parafoveal thickness up to day 9 postoperatively, and then only a slight decrease in the thickness at day 37.

Analyses of the changes in the superficial plexuses showed that the postoperative decrease of the FAZ area can be fit by a hyperbolic curve (Figure 2; $R^2 = 0.993$) . The area of the FAZ of the superficial plexus was 0.336 mm^2 preoperatively, and 0.285 mm^2 on day 1, 0.262 mm^2 on day 2, 0.212 mm^2 on day 9, and 0.209 mm^2 on day 37. The area of the FAZ in the normal fellow eye was 0.378 mm^2. The OCTA images of the superficial and deep plexuses and the horizontal cross sectional SS-OCT image of the normal fellow eye are shown in Figure 3.

The sequential horizontal cross sectional SS-OCT images during the follow-up period are shown in Figure 4. The preoperative OCT image showed that the foveal contour was normal. After the surgery, the parafoveal thickness was increased, and the foveal contour became steeper.

The thickness of the different retinal layers preoperatively and at day 37 postoperatively determined by the horizontal (top) and vertical lines (bottom) at 0.5 mm from the foveal center are shown in Figure 5. The thicknesses of the RNFL, GCIPL, and INL were increased postoperatively.

Discussion

We presented a case in which the FAZ area decreased and the parafoveal inner retina thickness increased after the vitrectomy with ILM peeling on an eye with a thin ERM and a normal foveal contour. There are three possible causes for the decrease of the FAZ area.

First, the release of the traction by the ERM may have caused the decrease. The preoperative surface maps showed that the parafoveal region was thicker in the affected eye than in the normal fellow eye although the foveal contour was normal. In addition, the FAZ area of the affected eye was similar in size with that of the normal fellow eye. It is possible that the thin ERM had influenced the parafoveal thickness, but the FAZ size and the foveal center thickness were unaffected. Thus, it seems unlikely that the release of the traction caused the decrease in the FAZ size.

Second, a growth of the capillaries toward the foveal center may have occurred after the ILM peeling. During the development of the human retina, the area of the FAZ is demarcated before the foveal pit forms. The FAZ is first observed at 26 weeks of gestation, and no vessel overgrowth is observed until birth. The FAZ area expands to the adult size of 500 to 700 μm at 15 months after birth as the foveal pit widens by remodeling.[12] No vessel overgrowth is observed during this process. It is less likely that an extension of the capillaries inside the FAZ occurs postnatally even after surgical procedures.

Third, the surgical procedures, ie, the vitrectomy and the ILM peeling, may have caused the FAZ area to decrease in size. Although it is difficult to distinguish the effects of each procedure, the surgical procedures may be partly responsible for the FAZ area decrease. The increase in the parafoveal inner retinal thicknesses may be due to a transient subclinical macular edema resulting from the ILM peeling.

The ILM peeling may cause a centripetal movement of the parafoveal inner retinal layer. The foveal capillaries run in the inner retinal layers, and the capillary network at the foveal margin forms the FAZ border. The capillary network delineating the FAZ border may have moved centripetally along with the inner retinal layers. This suggestion may also help explain the postoperative increase in the parafoveal thickness.

An inner retinal movement toward the foveal center would lead to a reduction in the FAZ area and cause more retinal cells to be packed in the parafoveal regions leading to an increase of the retinal thickness. In fact, the smaller FAZ area has been reported in other studies to be associated with an increase in the foveal thickness.[5-6,7-11] Also, an increase in the central macular thicknesses has been reported after ILM peeling in eyes treated for several macular diseases.[13-18]

One question raised from this possibility is why there is a centripetal retinal movement after ILM peeling. The ILM may have some intrinsic forces stretching the retina centrifugally and the removal of ILM may eliminate such forces leading to a centripetal movement. Additional studies need to be performed to determine why this occurs.

The structural changes to the Mueller cells may be a key factor influencing the inner retinal movement. The Mueller cells extend vertically for the full thickness of the retina, except for the foveal center, and they stretch eccentrically from the foveal center to the parafoveal region.[19] The footplates of the Mueller cells form the ILM. Thus, the structural changes in the Mueller cells after ILM peeling may be involved in the retinal movement.

The study has several limitations. First, the findings were made on only one eye. Thus, the examinations of a larger number of patients are needed. Second, longer follow-up periods and further studies are needed to determine the effects on the functional outcomes.

In conclusion, we observed a single case that FAZ area decreased after vitrectomy with ILM peeling. It may indicate that surgery can affect the morphology of the inner retina. However, the exact mechanisms causing these changes were not determined from the results of this single case. Our findings demonstrate the ability of OCTA in providing *en face* images that can be used to analyze the changes in the inner retinal area including the FAZ. Further studies are needed to determine the underlying mechanisms for the retinal movements.

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Increase in Average Foveal Thickness after Internal Limiting Membrane Peeling

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Abstract
Purpose :
To report the findings in three cases in which the average foveal thickness was increased after a thin epiretinal membrane (ERM) was removed by vitrectomy with internal limiting membrane (ILM) peeling.
Methods :
The foveal contour was normal preoperatively in all eyes. All cases underwent successful phacovitrectomy with ILM peeling for a thin ERM. The optical coherence tomographic (OCT) images were examined before and after the surgery. The changes in the average foveal (1mm) thicknesses and the foveal areas within 500μm from the foveal center were measured. The postoperative changes of the inner and outer retinal areas determined from the cross-sectional OCT images were analyzed.
Results :
The average foveal thickness and the inner and outer foveal areas increased significantly after the surgery in each of the three cases. The percentage increase in the average foveal thickness relative to the baseline thickness was 26% in Case 1, 29% in Case 2, and 31% in Case 3. The percentage increase of the foveal inner retinal area was 71% in Case 1, 113% in Case 2, and 110% in Case 3, and the percentage increase of the foveal outer retinal area was 8% in Case 1, 13% in Case 2, and 18% in Case 3.
Conclusions :
The increase in the average foveal thickness and the inner and outer foveal areas suggests that a centripetal movement of the inner and outer retinal layers toward the foveal center probably occurred due to the ILM peeling.

Introduction

Several authors have reported that the central fovea is thicker after internal limiting membrane (ILM) peeling than without ILM peeling.[1-5] However, these studies were conducted on eyes with macular diseases such as macular hole (MH),[1,2] epiretinal membrane (ERM),[2-4] and macular edema.[5] The effects of ILM peeling on the average foveal (1mm) thickness in a normal healthy eye has not been determined.

We performed vitrectomy with ILM peeling on these three eyes with a thin ERM and a normal foveal contour. Optical coherence tomography (OCT) was used to analyze the average foveal thicknesses and areas before and after the surgery.

Methods

The 3 eyes underwent successful phacovitrectomy with removal of the thin ERM and ILM peeling. The sequential changes in the average foveal thickness were determined by swept-source optical coherence tomography (SS-OCT; Topcon, DRI OCT-1 Atlantis, Tokyo, Japan). A written informed consent was obtained from all patients for data collections and the use of clinical data in research studies. This study followed the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of Kami-iida Daiichi General Hospital.

The retinal surface maps were reconstructed from the 3-dimensional cube scans, and the macular cube scans were used to measure average foveal thickness. The central and the inner four sectors as defined by the Early Treatment Diabetic Retinopathy Study (ETDRS) were analyzed. The outer four sectors were not analyzed because of the presence of perifoveal subretinal fluid due to rhegmatogenous retinal detachments (RRDs) in two eyes. The ratio of the temporal to nasal thicknesses (T/N ratio) was used to compare the temporal and nasal differences in the thicknesses after the vitrectomy with ILM peeling.[2,6]

The vertical and horizontal B-scan images through the foveal center were used to measure the thicknesses of the different retinal layers. The foveal areas of the horizontal and the vertical cross sectional areas with a radius of 500μm from the foveal center were measured. This area was bordered vertically by the vitreomacular interface and the ellipsoid zone of the photoreceptors and laterally at 500μm temporal, nasal, superior, and inferior to the foveal center. The area from vitreomacular interface to the inner nuclear layer was used to determine the foveal inner retinal area,[7] and the remaining area from the outer plexiform layer to the ellipsoid zone of the photoreceptors was used to determine the foveal outer retinal area.

The foveal outer and inner areas were measured using horizontal and vertical OCT cross sectional images of the foveal center to the temporal, nasal, superior, and inferior margins located 500μm from the foveal center. The values at 1 mm section centered on a foveal pit for horizontal and vertical OCT cross sections were averaged to obtain measurements for the foveal sectors.

The OCT images of 1:1 μm setting rather than 1:1 pixel settings were used for the measurements of the areas of the fovea. The areas were measured by manual segmentation with the ImageJ software (National Institutes of Health, ImageJ, Bethesda, MD, USA) . The areas of retinal selections for the foveal inner and outer retinal areas are shown in Figure 1. The retinal areas were

reported in mm^2.

Results

The clinical characteristics of the 3 cases are summarized in Table 1. Three cases of thin ERM were adopted in our study because the foveal contour was normal and the patients had no systemic diseases resulting in retinal diseases such as uncontrolled hypertension and diabetes mellitus. All of the cases underwent phacoemulsification, intraocular lens implantation followed by vitrectomy, ERM removal, and brilliant blue G (BBG) -assisted ILM peeling within the vascular arcade. Cases 1 and 2 had a peripheral RRD without macular detachment which was also treated during the surgery. In these two cases, the retina was tamponaded with SF6 at the completion of the surgery, and the patients were instructed to maintain a face-down position for 1 week postoperatively. The retina was reattached in both cases.

The sequential changes of the foveal area in the retinal surface maps and OCT images of Case 1 are shown in Figure 2. The diameter of the foveal pit became smaller, and the parafoveal thickness increased starting from the first postoperative week. A thinning in the temporal area and a thickening in the nasal area were observed.

The vertical and horizontal B-scan images of Case 2 preoperatively and at 6 months postoperatively are shown in Figure 3 (top right and top left) . The vertical and horizontal B-scan images of Case 3 preoperatively and 1 month postoperatively are shown in Figure 3 (bottom right and bottom left).

The changes in the average foveal thickness during the follow-up period for each case are shown in Figure 4. All of the eyes had an increase in the average foveal thickness relative to the baseline. The percentage increase at the final visit was 26% in Case 1, 29% in Case 2, and 31% in Case 3, and the mean percentage increase of 28.6%.

The thicknesses of the inner four ETDRS sectors preoperatively and at the final visit postoperatively are shown in Figure 5 for each case. The mean percentage increase was 2.0% (all 2.0%) in the inner superior sector, -1.3% (range, -5 to 2%) in the inner temporal sector, 3.0% (range, 1 to 5%) in the inner inferior sector, and 9.3% (range, 8 to ～ 10%) in the inner nasal sector. The preoperative T/N ratio was 0.97 in Case 1, 0.97 in Case 2, and 0.93 in Case 3, and the T/N ratio at the final visit were 0.87 in Case 1, 0.83 in Case 2, and 0.88 in Case 3.

The foveal inner and outer retinal areas preoperatively and at the final postoperative examination are shown in Figure 6 for each case. The area from the foveal center to the four points 500μm away from the center (superior, temporal, inferior, and nasal) were measured in the horizontal and a vertical OCT cross sectional images. The measurements obtained at 1 mm including the foveal center for both horizontal and vertical OCT cross sectional images were averaged to obtain the foveal section areas. Both the inner and outer retinal areas in each sector increased after the surgery in the three cases. The mean percentage increase in the foveal inner retinal area was 98.0% (range, 71 to 113%) in the foveal section. The mean percentage increase of the foveal inner retinal area was 89.3% in the superior sector, 126.3% in the temporal sector, 94.3% in the inferior sector, and 114.0% in the nasal sector.

The mean percentage increase of the foveal outer retinal area was 13.0% (range, 8 to 18%) in the foveal section. The mean percentage increase of the foveal outer retinal area was 12.7% in the superior sector, 15.0% in the temporal sector, 12.3% in the inferior sector, and 25.3% in the nasal sector.

Discussion

Our results showed that the average thickness of the fovea and the foveal inner and outer areas increased after the surgery in the three eyes. The mean percentage increase was 28.6% for the average foveal thickness, 98.0% for the inner retinal area, and 13.0% for the outer retinal area. These increases following the vitrectomy with ILM peeling suggest that the increase may be related to the ILM peeling.

In these three eyes, the surgical procedures included cataract surgery, vitrectomy, ERM removal, and ILM peeling with a staining of the ILM. A gas tamponade was used in the two cases with a RRD. In another case series, we performed vitrectomy with gas tamponade without ILM peeling in 17 eyes with a RRD and a normal foveal contour. We observed no change in a shape of the foveal pit (Unpublished data). We have also performed phacovitrectomy, ERM removal with BBG staining but without ILM peeling in a case of a thin ERM with a normal foveal contour. We did not observe any change in a foveal pit shape in this case (Unpublished data). It is more likely that the ILM peeling was the major factor contributing to the increase in the average foveal thickness and the smaller pit diameter. In addition, all three cases had a decrease of the T/N ratio after the surgery. It is most likely that the morphological changes in our cases were due to the ILM peeling procedures.

Retinal swelling associated with ILM peeling may be one reason for the increase in the average foveal thickness. The ILM is the basement membrane of the Mueller cells, and the Mueller cells play important roles in maintaining the physiology of the retina. A swelling of the nerve fiber layer occurs after ILM peeling during the early postoperative period.[8] Spaide stated that the removal of the ILM facilitates the flow of fluid into the inner retinal layer from the vitreous cavity because the ILM is a barrier for water transport between the inner retina and the vitreous humor.[4] Therefore, the foveal thickening during the early postoperative period might be related to the retinal swelling. However, the retinal swelling theory cannot explain the regional differences in the thickening such as the thinning in the inner temporal ETDRS sector as shown in Figure 4. It seems unlikely that the retinal swelling was a major reason for the increase in the average foveal thickness.

Movements of the retinal tissues associated with ILM peeling is well recognized to occur after treatment for several retinal diseases such as MH, [9,10,12,14,15] ERM,[11] and diabetic macular edema.[13] These retinal movements may contribute to the healing processes after the surgery. Our three cases had a thin ERM but the foveal contour was normal. Thus, changes in the average foveal thickness in these cases were more likely caused by the ILM peeling.

The average foveal inner retinal area increased after the surgery in all cases. The mean percentage increase was 98.0% in the foveal sector, and the mean percentage of increase at each of the four surrounding sectors ranged from 89% to 126%. Similarly, the foveal outer retinal area increased after the surgery in all cases. The mean percentage increase was 13.0% in the foveal sector, and the mean percentage increase at each of the four surrounding sectors ranged from 13% to 25%. The increase of the foveal area suggests that a lateral compression of the retinal cells occurred at the foveal center after the inner and outer retinal layers moved centripetally. We recently reported a case that suggested a centripetal movement of the inner retinal layers from the movement of the vessel bifurcation points after ILM peeling.[16] We also found a decrease in the size of the foveal avascular zone (FAZ) occurred postoperatively as seen by optical coherence tomography angiography in Case 3. The decrease in FAZ area suggests that a centripetal movement of retinal layers occurs after ILM peeling.[17]

Several studies have demonstrated a displacement of the fovea towards the optic disc after ILM peeling.[10,12-15] The present three cases also showed a reduction of the papillofoveal distances suggesting a centripetal retinal movement and retinal displacement toward the optic disc may have occurred simultaneously.

This study has several limitations. First, the findings were made in only three eyes. Although the foveal contour was normal in these eyes, the diagnosis for each eye was different (2 macular RRDs and 1 ERM) . Further data collection with the eyes of same diagnoses and non-ILM peeled controls are necessary to draw a statistical conclusion on this study, since our current data are simple calculations based on three cases. Second, the postoperative observation period varied among the cases. However, it is known that the average foveal thickness in ILM peeled eyes remains thick even after the long-term follow-up periods.[1,2,3,5,6,18,19]

In conclusion, our cases had an increase in the average foveal thickness and area after vitrectomy with ILM peeling. Our findings suggest that a centripetal movement of the foveal inner and outer retinal layers occurred after the ILM peeling. This centripetal movement may be a key factor for better central visual acuity after the ILM peeling. Further studies are needed to determine the underlying mechanisms of these retinal movements.

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Effect of Vitreomacular Adhesion and Vitreous Gel on Age-related Reduction of Macular Thickness

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Abstract

Objective : To investigate the effects of vitreomacular adhesion (VMA), vitreomacular separation (VMS), and absence of vitreous gel due to vitrectomy on macular thickness measured in the spectral-domain optical coherence tomographic (SD-OCT) images.
Design : A longitudinal, retrospective, observational study
Setting : Secondary, multicenter study.
Participants : Two hundred eighteen eyes of 218 healthy subjects and 119 vitrectomized eyes of 119 patients were studied. The healthy subjects were classified into a VMA group (54 eyes) and a VMS group (164 eyes), while the vitrectomized patients were classified into an ILM-on group (26 eyes) and an ILM-off group (93 eyes). In all participants, two Cirrus HD-OCT recordings were made with an average interval of 36 months (range, 24-60 months).
Primary and secondary outcome measures : The primary outcome measure was the rate of change of the macular thickness in the central sector. The secondary outcomes were the rates of change in the macular thickness in the inner four sectors.
Results : The annual rate of change in the macular thickness of the central sector was 0.76±1.8 μm/year in the VMA group, -0.58 ±2.3 μm/year in the VMS group, -1.57±1.9 μm/year in ILM-on group, and -0.86±3.1 μm/year in the ILM-off group. There was a significant difference between the rate of central sector thickness change in the VMA and VMS groups (P=0.0001). The presence of VMA was a significant factor associated with an increase in the central sector thickness (P=0.0055). When the healthy and ILM-on groups were compared, the rate of a decrease in central sector thickness was faster in the ILM-on group (P=0.0043). Multiple regression analyses showed that not peeling the ILM during the vitrectomy was a significant factor associated with a decrease in the central sector thickness (P=0.044).
Conclusion : The presence of a VMA and a vitreous gel may help restrain the macular thickness reduction.

Article summary

The rate of macular thickness changes was determined in eyes with vitreomacular adhesion, with vitreomacular separation, and without vitreous gel due to vitrectomy in the spectral-domain optical coherence tomographic images. The macular thickness increased in eyes with vitreomacular adhesion in all sectors, while it decreased in eyes with vitreomacular separation and in vitrectomized eyes.
Strengths and limitations :
・The patients in vitrectomized groups were examined at least 1 year after the vitrectomy when the confounding effects of surgery were somewhat mitigated.
・The vitrectomized group had concomitant diseases that were treated during the surgery and this may have influenced the changes in the macular thickness independent of the vitreous separation.
・The sample size was different in each group with the ILM-on group being the fewest with 26 eyes.

INTRODUCTION

Histological studies have demonstrated that the thickness of the retinal ganglion cell and nerve fiber layers decrease with increasing age.[1-2] The results of several optical coherence tomographic (OCT) studies have shown that aging has different effects on the retinal thickness.[3-14] The disparities among these reports may be due to the differences in the characteristics of the subjects, the types of OCT devices used, the retinal thickness parameters measured, and study design.

The resolution of the spectral-domain optical coherence tomographic (SD-OCT) instruments have improved with faster scanning speeds compared to time-domain OCT instruments.[15] The most valid approach to examine the age-related reductions in the macular thickness is to examine the serial changes in the same eyes over time, i.e., a longitudinal study instead of a cross sectional study.

We hypothesize that the presence of vitreous gel prevents a decrease in macular thickness. Thus, the purpose of this study was to determine the rates of change in the average macular thicknesses in four groups of eyes; eyes with a vitreomacular adhesion (VMA), eyes with a vitreomacular separation (VMS), eyes after vitrectomy with ILM peeling (ILM-off), and eyes after the vitrectomy without ILM peeling (ILM-on). To accomplish this, SD-OCT images were obtained by the Cirrus HD-OCT with the macular change analysis program. The images were collected from each eye at two time points with an average interval of 36 months. The rate of change in the different macular sector thickness was determined for these four groups.

MATERIALS AND METHODS

Participants

This was a longitudinal, retrospective study of subjects who were examined at the Shinjo Ophthalmologic Institute, Kami-iida Daiichi General Hospital and the Nishigaki Eye Clinic from October 2007 through December 2015. The subjects consisted of healthy controls and the patients who had undergone vitrectomy. The healthy controls (healthy group) were the patients who were being followed because of a cataract and did not have any retinal diseases. The healthy group was classified into a VMA group consisting of 54 eyes and a VMS group consisting of 164 eyes. The VMA status was confirmed to be the same in each of the SD-OCT image in all subjects of the healthy group.

The subjects without vitreous gel (vitrectomized group) had undergone vitrectomy with or without ILM peeling for several types of retinal diseases. The first measurement was made at least 1 year after the vitrectomy. The vitrectomy was performed on 110 eyes with a macular hole (MH), 5 eyes with a rhegmatogenous retinal detachment without involvement of the macula, and 4 eyes with vitreous hemorrhage.

A signed informed consent was obtained from all the participants for the procedures used during the examinations. The Ethics Committee of each hospital approved the protocol for this study, and all of the procedures adhered to the tenets of the Declaration of Helsinki.

Examinations

Each of the participant had a comprehensive ophthalmological examination including measurements of the refractive error, best-corrected visual acuity (BCVA) with a Landolt chart at 5 m, axial length by ocular biometry (IOL Master; Carl Zeiss Meditec), and intraocular pressure with a Goldmann applanation tonometer. In addition, the eyes were examined by slit-lamp biomicroscopy, dilated indirect slit-lamp biomicroscopy with and without contact lenses, indirect ophthalmoscopy, and SD-OCT.

Inclusion and Exclusion Criteria

The inclusion criteria for both groups were OCT image signal intensity ≥7, axial length <28.00 mm, and age ≥56-years at the time of the first OCT measurements. The inclusion criteria for the healthy group were BCVA ≥20/20, no significant cataract, and normal foveal contour. The inclusion criteria for the vitrectomized group were outpatient visit continued >3 year after the vitrectomy with OCT images available at each visit and the VMA status remain unchanged at these visits.

The exclusion criteria for both groups were persistent centering and segmentation errors. In addition, the subjects with any ocular or systemic disorders that could affect the retinal thickness, e.g., glaucoma, optic nerve diseases, and diabetes mellitus were excluded. The exclusion criteria only for the healthy group were unclear VMA status, i.e., cases in which full adhesion or detachment of the posterior vitreous could not be determined, vitreomacular traction, foveal deformation, and the change in VMA status at second OCT scan. The exclusion criteria only for the vitrectomized group was outpatient visit continued <3 year after the vitrectomy.

Surgical Treatments

All surgeries were performed by one surgeon (NO). All phakic patients underwent pars plana vitrectomy with phacoemulsification and implantation of a posterior chamber intraocular lens. The posterior hyaloid membrane and vitreous gel were removed, and the ILM was made visible with triamcinolone acetonide and peeled for three disc diameters around the fovea. ILM peeling was performed on 93 eyes on all eyes with a MH, and the ILM was not peeled in 26 eyes. In the MH eyes, sulfur hexafluoride gas was used for tamponade, and the patients were instructed to maintain a prone position for 7 days.

HD-OCT Recordings

The Cirrus HD-OCT (Carl Zeiss Meditec Inc, Dublin, California, USA) was used to obtain axial images of the vitreoretinal interface. At least 5 B-scan images of 6 mm in length passing through the fovea along the horizontal and vertical axes were recorded with 4096 A-scan resolution and 0.25-mm intervals between neighboring B-scans. The average regional thicknesses of the Early Treatment Diabetic Retinopathy Study (ETDRS) sectors and 6 x 6-mm macular cube scans were composed of 200 B-scans and 200 A-scans centered on the fovea. Experienced OCT examiners scanned the retina at least 3 times to obtain images with signal intensity of ≥7. The images with centering or segmentation errors were excluded. The retinal thickness was automatically measured with the vitreoretinal interface as the inner border of the retina and the anterior border of the RPE as the outer border of the retina.

The average increase or decrease in the retinal thickness/year was determined using the Cirrus macular change analysis program. The macular change analysis program compares the OCT scans from consecutive examinations. The retinal alignment was based on the vessel landmarks to the initial OCT images, which was done automatically. The analyses were made on the central and the inner four ETDRS sectors with a mean interval of 36 months (range, 24-60 months) between two observational scans. For the vitrectomized group, a first OCT scan was recorded at least 1 year after the vitrectomy. Then, a second OCT scan was recorded at least 2 years after the first scan. Therefore, all patients from this group were examined for at least 3 years after the vitrectomy. When several OCT scans were available from the same patient, only the latest scan was selected for the analysis.

Statistical Analyses

Unpaired *t* tests were used to determine the significance of the differences in the numerical data, and chi-square tests were used for the categorical data between each group. Multivariate regression analyses were used to determine the associations between the rate of macular thickness change and the clinical factors, e.g., sex, age, axial length, presence of VMA, and ILM peeling. A *P* value <0.05 was accepted as statistically significant. Statview software version 5.0 (SAS Institute, Inc, Cary, North Carolina, USA) was used for the statistical analyses.

RESULTS

The baseline characteristics of the subjects and the mean rates of macular thickness change in the VMA, VMS, ILM-on, and ILM-off groups are shown in Table 1. The MHs were closed in all 110 eyes after the vitrectomy, and no surgical complications were observed in the vitrectomized group. For the healthy group, the central and inner four sectors were significantly thinner in the VMS group than in the VMA group. For the vitrectomized group, the rate of macular thickness decrease in the central sector was faster in the ILM-on group than in the ILM-off group. In contrast, the rate of macular thickness decrease in the inner four sectors was slower in the ILM-on group than in the ILM-off group, but the decrease was only significant in the inner inferior sector ($P = 0.032$). The subjects in the VMS group were significantly older than those in the VMA group ($P < 0.0001$).

Table1. Baseline characteristics and macular thickness changes

	Healthy group			Vitrectomized group		
	VMA (n=54)	VMS (n=164)	*P* value	ILMon (n=26)	ILMoff (n=93)	*P* value
Women no. (%)	31(57.4)	118(72.0)	0.046[a]	14(53.8)	66(71.0)	0.10[a]
Age (years)	65.2±6.4	69.3±6.5	<0.0001[b]	69.9±7.3	68.4±6.0	0.27[b]
range	(56-84)	(56-86)		(56-80)	(57-80)	
Axial length (mm)	23.5±1.2	23.6±1.2	0.95[b]	24.1±1.6	23.3±1.3	0.012[b]
Range	(21.0-26.1)	(21.3-27.1)		(22.1-27.0)	(21.5-27.7)	
Sectors (μm/year)						
Central	0.76±1.8	-0.58±2.3	0.0001[b]	-1.57±1.9	-0.86±3.1	0.27[b]
inner superior	0.23±1.8	-0.97±2.1	0.0002[b]	-1.95±2.0	-2.14±2.3	0.69[b]
inner temporal	0.096±1.6	-0.92±2.1	0.0016[b]	-1.51±1.8	-2.47±2.3	0.054[b]
inner inferior	0.20±1.5	-1.13±2.1	<0.0001[b]	-1.29±1.8	-2.40±2.4	0.032[b]
inner nasal	0.072±1.6	-0.94±2.0	0.0011[b]	-1.51±1.9	-1.72±2.5	0.68[b]

VMA=vitreomacular adhesion
VMS=vitreomacular separation
ILM=internal limiting membrane
[a] Chi-square test
[b] Unpaired *t* test

The results of the multiple regression analyses for macular thickness changes among the healthy group are shown in Table 2. The presence of VMA was a significant factor associated with the increase in macular thicknesses in all sectors ($P < 0.0002$ to 0.0055).

Table 2. Multiple regression analysis for macular thickness changes among healthy group

	central		superior		temporal		inferior		nasal	
	β	*P* value	β	*P* value	β	*P* value	β	*P* value	β	*P* value
Women	-0.041	0.58	-0.022	0.76	-0.066	0.38	-0.056	0.45	-0.016	0.83
Age	-0.11	0.13	-0.085	0.23	-0.032	0.66	-0.060	0.40	-0.030	0.68
Axial length	-0.13	0.087	-0.12	0.12	-0.088	0.25	-0.073	0.33	-0.077	0.31
Presence of VMA	0.20	0.0055	0.24	0.001	0.20	0.0048	0.27	0.0002	0.22	0.0021

VMA=vitreomacular adhesion

The results of the multiple regression analysis for macular thickness changes in the vitrectomized group are shown in Table 3. The ILM peeling was a factor significantly associated with a

decrease in macular thicknesses in the inner temporal and inferior sectors (P = 0.0096 and P = 0.0047, respectively). The central sector thickness was not affected by the ILM peeling (P = 0.58).

Table 3. Multiple regression analysis for macular thickness changes among vitrectomized group

	central		superior		temporal		inferior		Nasal	
	β	P value	β	P value	β	P value	β	P value	β	P value
Women	-0.005	0.96	0.15	0.15	0.024	0.81	0.10	0.32	0.10	0.32
Age	-0.19	0.053	-0.19	0.048	-0.17	0.083	-0.20	0.038	-0.079	0.42
Axial length	-0.058	0.60	-0.18	0.11	-0.21	0.059	-0.13	0.21	-0.22	0.049
ILM peeling	0.054	0.58	-0.13	0.17	-0.25	0.0096	-0.27	0.0047	-0.11	0.25

ILM=internal limiting membrane

The baseline characteristics and macular thickness changes in the healthy and the ILM-on groups are shown in Table 4. The rate of macular thickness decrease was significantly faster in the ILM-on group than in the healthy group (VMA+VMS groups).

Table 4. Baseline characteristics and macular thickness changes in healthy and ILM-on group

	Healthy (n=218)	ILM-on (n=26)	p value
Women no. (%)	149 (68.3)	14 (53.8)	0.14[a]
Age (years)	65.3±6.7	69.9±7.3	0.24[b]
range	(56-86)	(56-80)	
Axial length (mm)	23.6±1.2	24.1±1.6	0.035[b]
range	(21.0-27.1)	(22.1-27.0)	
Sectors (μm/year)			
Central	-0.25±2.2	-1.57±1.9	0.0043[b]
inner superior	-0.68±2.1	-1.95±2.0	0.0038[b]
inner temporal	-0.67±2.1	-1.51±1.8	0.046[b]
inner inferior	-0.80±2.1	-1.29±1.8	0.24[b]
inner nasal	-0.69±2.0	-1.51±1.9	0.049[b]

ILM=internal limiting membrane
[a]Chi-square test
[b]Unpaired *t* test

The results of the multiple regression analysis for macular thickness changes in the healthy and the ILM-on group are shown in Table 5. The rate of decrease in the macular thickness was significantly faster in the central and the inner superior sectors of the ILM-on group (P = 0.044 and P = 0.028, respectively).

Table 5. Multiple regression analysis for macular thickness changes in healthy and ILMon group

	central		superior		temporal		inferior		nasal	
	β	P value	β	P value	β	P value	β	P value	β	P value
Women	-0.058	0.42	-0.019	0.79	-0.079	0.28	-0.081	0.27	-0.025	0.73
Age	-0.16	0.017	-0.13	0.058	-0.064	0.35	-0.12	0.087	-0.066	0.33
Axial length	-0.13	0.083	-0.16	0.028	-0.10	0.18	-0.086	0.25	-0.12	0.11
ILM-on	-0.14	0.044	-0.15	0.028	-0.11	0.092	-0.056	0.41	-0.11	0.10

ILM=internal limiting membrane

The rates of macular thickness changes in the central sectors are shown in Figure 1. The thickness of the central macular sector increased in the VMA group, while it decreased in the VMS, ILM-on, and ILM-off groups. The decrease in the central sector thickness was fastest in the ILM-on group.

Also, we have provided Supplementary Table 1-5 showing the data from Table1-5 in percentage of the macular thickness changes.

DISCUSSION

We determined the rates of macular thickness change in the central and inner four ETDRS sectors obtained by the Cirrus macular change analysis program from longitudinal measurements of the healthy and the vitrectomized subjects. The macular change analysis program compared the thickness of identical macular regions so even slight changes in the macular thickness over time could be detected.

The macular thickness increased in all sectors in the VMA group with the rates ranging from 0.072 to 0.76 μm/year. Batta et al[16] suggested that the retinal nerve fiber layer (RNFL) is thicker in patients with a partial posterior vitreous detachment (PVD) than in controls without a partial PVD. Vitreous traction on the macular area may be the reason for the increase in macular thickness.[16] In contrast, the macular thickness decreased in all sectors of the VMS group with the rates ranging from -0.58 to -1.13 μm/year. Multiple regression analyses showed that the presence of VMA was a significant factor that restricted the reduction of the macular thickness in all sectors. This suggests that the presence of the vitreous gel and VMA may be factors restraining the age-related reduction of the macular thickness.

In the VMS group, the mean rate of change in the central sector was slower at -0.58 μm/year than the inner four sectors at -0.92 to -1.13 μm/year. The extrafoveal thickness decreased more with aging than the central foveal thickness. The reason for this is the anatomical effects of aging on the macular region. The inner retinal layer is thinnest in the central fovea while the outer retinal layer is thickest in this area.[13] The inner retinal thickness over the whole macular area decreased with aging while the outer retinal thickness did not decrease with aging.[13] Therefore, some authors have reported that the extrafoveal thickness which is affected by the inner retinal thickness decreased with aging,[5,6,8,10-12] while the central foveal thicknesses did not change with aging.[4,7-9,14]

Other authors have reported that the central foveal thickness increases with increasing age.[5,10,11] The significant differences in the mean ages of the VMA and VMS groups may have affected our results. However, the multiple regression analyses of the healthy group showed that the age was not significantly associated with the macular thickness. Instead, the presence of VMA was a significant factor associated with the macular thickness increase of each sector. The results of the earlier studies showed that the central foveal thickness increased with increasing age in both VMA and VMS groups. Thus, the proportion of the individuals with VMA may be higher in these reports leading to the observed increase in central sector thickness.

In the vitrectomized group, the macular thickness decreased in all of the sectors. The rate of macular thickness decrease was faster in the central sector of the ILM-on group at -1.57 μm/year. In contrast, the rate of decrease was faster in the inner four sectors of the ILM-off group at -1.72 to -2.47 μm/year. ILM peeling tended to increase the rate of macular thickness reduction in the inner temporal and inferior sectors (Table 3). However, the ILM-on group consisted of only 26 eyes (21.8% of all vitrectomized eyes) , so the results may show significant differences in other sectors if more data were available in this group.

The eyes with and without vitreous gel (the healthy group and the ILM-on group respectively) were compared to analyze if the presence of the vitreous gel prevented the decrease in macular thickness. The ILM-off group was excluded from this comparison because the macular thicknesses were shown to be significantly affected by ILM peeling on Table 3. When the healthy and the ILM-on groups were compared, all sectors except the inner inferior sectors decreased at significantly faster rates in the ILM-on group. In contrast, multiple regression analyses showed that leaving ILM-on during the vitrectomy was significantly associated with the decrease in the central and inner superior sector thicknesses. Although there are differences in the rate of decrease in each sector, the removal of vitreous gel seems to facilitate the macular thickness decrease. Other factors contributing to the macular thickness decrease may be surgical damage, natural course of the disease, secondary glaucoma, and the absence of the vitreous gel traction after the vitrectomy although it was difficult to measure the effects of these factors unambiguously.

Although our study showed that the annual change in macular thicknesses for each group was significant, the amount of change was very small (mostly <1 μm). Our hypothesis was based on the idea that the retinal oxygen distribution change occurring after the vitreous gel removal will eventually lead to retinal thinning. Vitrectomy leads to an increase in the retinal oxygen concentration.[17] Elevated intraocular oxygen levels tend to be beneficial for the resolution of macular edema, but may contribute to the development of nuclear cataract and primary open-angle glaucoma.[18-20] An intact vitreous gel may play an active role in preventing retinal tissue damage from free oxygen radicals.[19,20] As the vitreous gel undergoes liquefaction by aging or surgical removal, the fluid that replaces the vitreous gel promotes a rapid distribution of oxygen within the eye through fluid mixing[18-20] leading to a wider area of retinal tissue damages and thinning by exposure to free radicals. Thus, we hypothesized that the presence of vitreous gel may help restrain the age-related reduction of the macular thickness. Still, the reason for the faster rate of macular thickness reduction in the vitrectomized group compared to the VMS group was not definitively determined.

Lee et al[21] reported that vitrectomy alone does not affect the RNFL thickness. In our study, the subjects in the vitrectomized group were those who had undergone vitrectomy for several non-degenerative retinal diseases and were followed for at least 1 year after the surgery before the first OCT recordings were

made. It is unlikely that damages from the vitrectomy affected the mean rate of macular thickness change. Several studies have reported on a significant association between open-angle glaucoma and vitrectomy.[22-25] The 1-year results of the Prospective Retinal and Optic Nerve Vitrectomy Evaluation (PROVE) Study showed an inferior peripapillary RNFL thinning indicating an early glaucomatous damage was observed in vitrectomized patients.[25] In the current study, glaucomatous changes were not observed in the vitrectomized group.

The strength of this study is that the patients in the vitrectomized groups were examined at least 1 year after the vitrectomy when the confounding effects of the surgery were somewhat mitigated. There are several limitations to this study. First, the vitrectomized group had concomitant diseases, mostly MHs, that were treated during the surgery and this may have influenced the changes in the macular thickness independent of the vitreous separation. Second, we examined subjects who were ≥56-years-of-age, and the rates of macular thickness reduction may not apply to younger individuals. Third, the results need to be confirmed by a larger sample size because the numbers of eyes in the VMA group as well as in the ILM-on group were small. Fourth, we measured the thickness of the entire retina, and did not measure the thickness of each layer. Some authors have reported that individual retinal layers were selectively affected by age.[12,13] Future studies should be designed to determine whether the reduction in the macular thickness is related to a specific retinal layer.

In conclusion, our results indicated that the age-related reduction of macular thickness was influenced by the presence of a posterior VMA and the presence of vitreous gel. We suggest that the VMA and vitreous gel may help restrain the age-related reduction of the macular thickness. Further studies are necessary to confirm our findings.

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Similarity of symptoms between transient epileptic amnesia (TEA) and Lewy body disease (LBD)

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Abstract
Epilepsy with the main symptom of amnesia is known as transient epileptic amnesia (TEA) . Dementia with Lewy bodies (DLB) is the second most common form of neurodegenerative dementia. The concept that Lewy body disease (LBD) includes Parkinson's disease with dementia and DLB was proposed in the 2005 revision of the Clinical Diagnostic Criteria. We describe a woman with cognitive impairment, olfactory dysfunction, and reduced ^{123}I-meta-iodobenzylguanidine uptake on myocardial scintigraphy. However, the patient and her family/friends were unaware of parkinsonism, visual hallucinations, or epilepsy for a long period. After syncope

occurred twice with a short interval, electroencephalography revealed sharp waves from the bilateral frontal to parietal lobes, indicating a diagnosis of TEA. The present case prompted us to compare the symptoms of TEA with the clinical diagnostic criteria for DLB, revealing their similarity. We also discuss whether LBD may cause TEA, rather than these conditions showing an incidental association.

INTRODUCTION

Amnesia caused by temporal lobe epileptic seizure is well known, but another type of epilepsy with the main symptom of amnesia also exists. In the late 1990s, Kapur et al. and Zeman et al. reported on the clinical features of transient epileptic amnesia (TEA).[1-3] Patients with TEA almost always have an interesting type of memory disorder, in which relatively long-term memory (for several weeks and/or months) is more severely affected than short-term memory (for several minutes and/or hours). This characteristic memory disorder is labeled "accelerated long-term forgetting (ALF)".[4]

Dementia with Lewy bodies (DLB) is the second most common form of neurodegenerative dementia, and it is characterized by symptoms such as visual hallucinations, parkinsonism, and olfactory dysfunction. Clinical diagnostic criteria for DLB were first published in 1995.[5] These criteria were revised in 2005, when Lewy body disease (LBD) was proposed as an entity including Parkinson's disease with dementia (PDD) and DLB.[6] In the revised criteria, PDD is differentiated from DLB by differences in the pattern of onset of motor symptoms and dementia, but many investigators have suggested that the two diseases are essentially the same and share the same pathological basis.

Lewy body disease is characterized by neuronal accumulation of alpha-synuclein and by the formation of Lewy bodies and Lewy neurites throughout the body, including in the central nervous system and the autonomic nervous system. Therefore, a variety of neurological and/or mental symptoms can occur at each stage of LBD.[7]

Here we report a female patient with memory disturbance similar to ALF, who lacked the core features for diagnosis of DLB in the 2005 revised guidelines (parkinsonism and visual hallucinations). On the other hand, she had olfactory dysfunction and reduced ^{123}I-meta-iodobenzylguanidine (MIBG) uptake on myocardial scintigraphy.

The present case prompted us to compare the symptoms of TEA with the 2005 clinical diagnostic criteria for DLB, revealing their similarity. We suggest that clinicians should pay more attention to the possible co-existence of TEA and LBD, because the symptoms of both diseases are often similar and it can be difficult to detect TEA in patients with LBD.

CASE REPORT

Written informed consent to the presentation of this report was obtained from the patient and her family. Minor modifications to the case details that did not interfere with important data were made to preserve anonymity.

A 67-year-old woman attended our memory clinic in 200X. She was on treatment with amlodipine besilate and pravastatin sodium for hypertension and hyperlipidemia, respectively. Electrocardiographic findings were within normal limits. She stated that her memory had become faulty and she had forgotten many actual events, such as having lunch with friends a few weeks ago, traveling with a friend a few months ago, and causing a traffic accident (without head trauma) while driving about four weeks ago. Neurological findings were within normal limits. For example, she could walk and turn quickly and had no rigidity of the extremities, with no parkinsonism being evident. Her Mini-Mental State Examination (MMSE) score was 29. Neither disorientation nor constructive apraxia were evident. She completed the clock-drawing test smoothly, and could correctly recall a sentence that she had been asked to memorize about 30 minutes before. Her Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS J-cog) score was 1.34 and she did not have visual hallucinations. Cranial magnetic resonance imaging (MRI) revealed no abnormalities. The Voxel-based Specific Regional analysis system for Alzheimer's Disease (VSRAD), which is a diagnostic aid for this disease, gave a Z-score of 1.04 for her entorhinal region. The patient apparently had disturbance of relatively long-term memory, but not short-term memory, which affected her recall of events from several weeks and/or months earlier. This type of memory impairment was not typical of Alzheimer's disease. She was asked to undergo follow-up evaluation every six months.

In 200X+1, she presented again with her family. This time, she had noted a decrease in the sense of smell, e.g., being unaware of the smell of burnt fish while cooking, or being able to eat vegetables which she previously thought had an unpleasant odor. Family members stated that she had difficulty with routine accounting tasks, often showed fluctuation of cognitive function, and easily became angry. The MMSE and ADAS J-cog scores were 29 and 5.4, respectively. There were no abnormal neurological symptoms/findings, including parkinsonism and visual hallucinations. Single-photon emission computed tomography (SPECT) revealed a decrease of blood flow in the bilateral temporal and occipital lobes, especially deep inside the temporal lobes. Uptake of MIBG on myocardial scintigraphy was abnormal, with reduction in the heart/mediastinum ratio (H/M ratio) to 1.25 (normal range : > 1.80) on early images and 1.04 (normal range : > 2.00) on delayed images.

She subsequently had 2 episodes of syncope within a short period, and she did not remember undergoing MIBG myocardial scintigraphy about one month before. Syncope is a characteristic symptom of DLB. However, electroencephalography (EEG) was performed for suspected epilepsy and sharp waves were detected from the bilateral frontal to parietal lobes.

Administration of levetiracetam was commenced and the dose was increased to 1500 mg/day, resulting in improvement of anterograde amnesia that was confirmed by questioning the patient and her family about life events after the start of levetiracetam treatment. Her syncope also resolved clinically. However, her lost memories were not restored and the olfactory dysfunction also persisted. She was diagnosed as having TEA with ALF and possible very early LBD.

About 6 months later, she developed a new condition unrelated to either epilepsy or neurodegenerative disease and moved to live with her oldest daughter.

DISCUSSION

We considered that this patient possibly had very early DLB for the following reasons. She had olfactory dysfunction. SPECT revealed reduced blood flow at the temporal and occipital lobes. In addition, myocardial scintigraphy revealed low MIBG uptake.

Although syncope is a characteristic symptom of DLB, the 2 episodes of loss of consciousness that occurred within a short period were probably caused by complex partial seizures (CPS). This conclusion is supported by the subsequent detection of abnormal sharp waves on the EEG and resolution of syncope after she started treatment with levetiracetam. Since her forgetfulness also improved with levetiracetam treatment, her episodic memory loss was thought to have been caused by unrecognized partial seizures and/or abnormal neuronal discharges without clinical seizures. These findings were compatible with a diagnosis of TEA.[3]

The present case raises questions such as whether DLB should be excluded because a patient only has symptoms of TEA (which are similar to those of DLB), whether the association of early DLB and TEA is incidental, or whether DLB and TEA are related disorders.

We investigated these issues by comparison of symptoms between TEA and DLB as detailed below.

1. Olfactory dysfunction

Although transient olfactory dysfunction and/or olfactory hallucinations have been described as symptoms of epileptic seizures, persistent olfactory impairment has not been recognized in association with TEA.[8] On the other hand, olfactory function is often disturbed in the early stage of DLB since the olfactory bulb and amygdala show early impairment in this disease.[7]

In this patient, persistent olfactory impairment might have been caused by an organic disorder of the olfactory bulb and/or amygdala rather than being a functional disorder due to epileptic seizures, because anti-epileptic therapy did not improve it. The amygdala is often considered to be the origin (focal point) in patients with partial seizures. Is it possible that accumulation of alpha-synuclein causes abnormal neuronal discharges? Is it also possible that abnormal discharges can result in structural damage to the amygdala? In our patient, SPECT images demonstrated a significant focal decrease of cerebral blood flow deep inside the temporal lobes (near the amygdala), suggesting a possibility that the amygdala might be an origin of the seizures.

2. Rapid eye movement sleep behavior disorders

Rapid eye movement sleep behavior disorders (RBD) are a characteristic symptom of LBD, which are classified as a supporting feature in the diagnostic criteria for DLB.[9] Patients with temporal lobe epilepsy sometimes develop RBD-like symptoms. If partial seizures occur during sleep, behavioral symptoms associated with this condition might be mistaken for symptoms of RBD. A definitive diagnosis of RBD requires overnight polysomnography to detect rapid eye movement sleep without atonia (RWA).[10] However, conducting this test is challenging in general hospitals so RBD tends to be diagnosed from symptoms, such as awakening easily or remembering dreams, and the correspondence of such symptoms with abnormal behavior.

3. Syncope and disturbance of consciousness
Syncope and/or disturbance of consciousness are essential symptoms of CPS. These symptoms often also develop in LBD because of autonomic neuropathy and/or fluctuating attention and alertness, and are classified as suggestive features in the diagnostic criteria for DLB. Differential diagnosis of these two conditions is difficult, requiring careful observation of other symptoms of autonomic dysfunction and the episodes of syncope.
4. Fluctuating cognition with pronounced variation in attention and alertness
Attention and alertness often vary in LBD. These symptoms are classified as core features in the clinical diagnostic criteria for DLB. However, attention and alertness will also tend to vary after partial seizures.
5. Visual hallucinations
Visual hallucinations are an important characteristic of DLB, and occurrence of such hallucinations is classified as a core feature. On the other hand, visual hallucinations also occur in patients with epileptic seizures. This similarity means that TEA is sometimes difficult to diagnose correctly.[11]
Thus, the symptoms of TEA and LBD are often similar, leading to difficulty in differential diagnosis, and possible complications of these diseases should also be considered.
Furthermore, rather than TEA and LBD being incidentally associated, abnormal discharge of neurons in the amygdala might occur because of pathologic changes related to accumulation of alpha-synuclein, which occurs in the early stage of LBD, resulting in TEA. Investigation of more patients will be needed to test this hypothesis.

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DISCLOSURE
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Effectiveness of low-dose pregabalin in three patients with Lewy body disease and central neuropathic pain

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Abstract
Many patients with Lewy body disease (LBD) complain of pain, and their pain may be associated with this disease. Recently, pain has become a focus of attention in Parkinson's disease (PD) , but there is little information regarding pain in patients who have dementia with Lewy bodies. We used pregabalin to treat three LBD patients with chronic pain that may have been related to degeneration of central neurons. All 3 patients responded well to pregabalin at 25 to 50 mg/day. To our knowledge, there have been no previous reports of pregabalin showing efficacy for central neuropathic pain in PD or LBD.

INTRODUCTION
Cognitive impairment is often observed in patients with Parkinson's disease (PD) , although this is contrary to the first report published by James Parkinson. In fact, approximately 30% of patients with PD have dementia and its prevalence is estimated to be at least 75% among those with a more than 10-year history of the disease.[1)]
Dementia with Lewy bodies (DLB) is the second most common type of neurodegenerative dementia, and is characterized by symptoms such as visual hallucinations and Parkinsonism. Clinical diagnostic criteria for DLB were first published in 1995.[2)] These criteria were revised in 2005, when Lewy body disease (LBD) was proposed as an entity that includes Parkinson disease with dementia (PDD) and DLB.[3)] In the revised criteria, PDD is differentiated from DLB based on differences in the onset of motor symptoms and dementia, but many investigators have suggested that the two diseases are pathologically or essentially the same. In fact, PD is often regarded as being included in the category of LBD. Many patients with LBD complain of pain, which is thought to be associated with this disease. While pain in patients with PD has recently been the focus of attention, there is still little information regarding pain in DLB patients.[4-8)] Pain related to PD may be multifactorial and associated with : 1) dystonic spasm, 2) musculoskeletal disorders, 3) radiculo-neuritic syndromes, 4) degeneration of central neurons, or 5) mental factors.[4-6)] However, the details of the mechanism involved remain to be clarified. Of the suggested mechanisms, pain related to central nervous system degeneration is characterized by : 1) stinging, numbness, or a burning sensation, 2) affects various sites such as the tongue, pharynx, back, pelvis, and vulva, and 3) is inconsistent with the anatomical dermatomes.[4-6)] Efficacy of drug therapy for this type of PD-related pain has not been established. Depending on their symptoms, some patients may respond to dopamine replacement therapy, antidepressants, anti-epileptic drugs, or anti-inflammatory analgesics, but more effective therapy for this pain is required. [9,10)]
We used pregabalin to treat 3 LBD patients with chronic pain persisting for years, which may have been related to central nervous system changes. In Japan, the standard dose of pregabalin for neuropathic pain is 300 to 600 mg/day. However, we found that a low dose pregabalin (25 to 50 mg/day) was effective for pain in these LBD patients.

CASE REPORTS
Informed consent to publish clinical information was obtained from the patients and their families. Minor modifications to data that did not interfere with this study were made to preserve the anonymity of these patients.

Case 1
The patient was a woman in her early 70s. There was no relevant past history. In 200X-3, she consulted the Department of Neurology at another hospital with the symptoms of weakness of the fingers, anorexia, cold sweats, lower abdominal pain, vulvodynia, and nocturia. Cranial magnetic resonance imaging

(MRI) did not reveal any abnormalities. She also attended the Departments of Cardiology and Gastroenterology, and underwent various examinations, but no abnormalities were identified. In 200X-2, she consulted the Department of Geriatrics at another hospital, but no abnormalities were detected. One month later, emergency admission to a third hospital was performed because of syncope. Although examinations did not reveal any abnormalities, "strange behavior" was noted during admission. She was referred to a psychiatric hospital and treatment was started with a diagnosis of senile depression. However, her condition deteriorated, with the onset of visual hallucinations and abnormal behavior at night. In 200X-2, she consulted the Department of Neurology at another hospital (the 5th). ^{123}I-IMP single-photon emission computed tomography and ^{123}I-meta-iodobenzylguanidine myocardial scintigraphy were performed, leading to a diagnosis of DLB. Since treatment of her visual hallucinations and abnormal nocturnal behavior was considered to be a priority, she was referred back to the psychiatric hospital. Treatment for DLB was started, but her symptoms progressed further. In 200X-2, she was admitted to the hospital. After more than 1 year as an inpatient, there was no improvement. In 200X, her family brought her to our department. On examination, her general condition was poor and she was confined to a wheelchair. Severe muscular rigidity was observed in the extremities and articular contractures were also noted. She was unable to stand up without assistance. Although there was no marked loss of recent memory or disorientation, she had visual hallucinations ("I see babies and children", "pieces of white paper are flying everywhere") and auditory hallucinations ("I can hear children singing or military songs"). She also complained of pain and a cold sensation of the lower abdomen, vulva, and lower limbs. The Mini-Mental State Examination (MMSE) score was 18, suggesting marked constructive apraxia. On cranial computed tomography (CT), the hippocampus was intact and ischemic changes of the cerebral white matter were not marked. Her treatment at the psychiatric hospital was donepezil at 3 mg, L-Dopa at 100 mg, risperidone at 0.5 mg, mianserin at 30 mg, zopiclone at 7.5 mg, and an H2 blocker. Her family did not want her to remain in the psychiatric hospital, and switched to outpatient care by our department. After discharge from the psychiatric hospital, her regimen was changed, with risperidone, mianserin, zopiclone, and the H2 blocker being discontinued. In addition, the doses of donepezil and L-Dopa were gradually increased. A day care service and physical therapy were introduced through utilization of nursing insurance, and the family was given guidance about exercise and rehabilitation.

After 2 years, improvement of walking was achieved and she was able to go to the toilet without assistance. The MMSE score was 21. In addition to marked improvement of her general condition, behavioral and psychological symptoms of dementia such as visual hallucinations and hypobulia also showed improvement. However, there was persistence of the lower abdominal/vulvar/femoral pain, which she had mentioned from 200X-3. She reported "intolerable pain with a cold sensation", "sudden pain", "pain persisting for a few hours", and "pain disturbing sleep". These symptoms suggested that her pain was related to an abnormality of the central nervous system, i.e., central neuropathic pain. After obtaining informed consent, pregabalin was administered at 50 mg/day. At the next consultation, there was reduction of the pain. Her family reported marked improvement after 1 to 2 weeks, stating that "she could sleep well at night", "there were no complaints of pain", and "our stress was rapidly reduced".

During subsequent follow-up for 1 year, there was no recurrence of pain without other analgesics. There were no adverse reactions of pregabalin, such as aggravation of cognition, behavioral and psychological symptoms, and Parkinsonism. She became able to travel, and there was marked improvement of the quality of life (QOL).

Case 2

The patient was a woman in her early 70s with a history of PD. She had been receiving treatment for PD for at least 10 years from the Department of Neurology at a university hospital. Recently, abnormal behavior had appeared, and her family had taken her to a memory clinic. However, her symptoms did not improve. In 200X, she was brought to our department in a wheelchair. On examination, prominent tremor of the extremities was observed. She was unable to walk without assistance. While there was no marked loss of recent memory or disorientation, she complained of visual hallucinations ("I can see a decapitated head", "a large number of people are coming here"), as well as severe pain and numbness of the limbs. The MMSE score was 24, suggesting marked constructive apraxia. On cranial CT, the hippocampus was intact and ischemic changes of the white matter were not prominent. Her medications prescribed by the memory clinic were as follows : galanthamine at 8 mg, L-Dopa at 900 mg, entacapone at 600 mg, haloperidol at 0.2 mg, sertraline at 25 mg, nitrazepam at 5 mg, clonazepam at 0.5 mg and a nonsteroidal anti-inflammatory drug (NSAID) as required. These medications were changed, with administration of haloperidol and sertraline being discontinued, while the doses of L-Dopa and entacapone were decreased. The dose of galanthamine was gradually increased, while zonisamide, istradefylline, and Yokukansan (a Japanese herbal medicine) were also administered.

After 2 years, hallucinations and symptoms of Parkinsonism showed improvement, and the MMSE score was 27. However, severe pain and numbness of the limbs persisted. She reported "severe pain like an electric shock", "pain exacerbated by touch", "sudden pain", "pain persisting for a few hours", and "oral pain (of the oral mucosa and tongue)", suggesting central neuropathic pain. Pregabalin was administered at 25 mg/day. After 2 weeks, her pain decreased to a tolerable level. According to the family, there were no further complaints of pain, which she had persistently mentioned for at least 5 years, and the NSAID was no longer necessary. Nine weeks after starting treatment, the patient noted improvement of the pain and did not wish to increase the dose of pregabalin.

During subsequent follow-up for 6 months, the improvement was maintained without adverse reactions of pregabalin. Improvement of sleep was also achieved, with nitrazepam and clonazepam no longer required.

Case 3

The patient was a man in his late 70s with a history of diabetes mellitus. Visual hallucinations had developed during the past 4 years and he often saw cats, but had not told his wife. His visual hallucinations had become more severe during the past 3 months, including visions of tigers and strangers. Auditory hallucinations (cries and whistles) also occurred frequently. Anxiety and fear affected his QOL. In 200X, he consulted our department, complaining of "being unable to distinguish reality from dreams", "being in a daze", "difficulty with walking", "disturbance of hand movements", and pain and numbness of the lower abdomen, lower back, and bilateral lower limbs. On examination, there was mild lead pipe rigidity of the bilateral upper extremities, as well as impairment of postural reflexes, parkinsonian gait, and myoclonus of the left lower limb. The MMSE score was 12. Cranial MRI revealed no abnormalities, except for slight ischemic changes in the cerebral white matter. Treatment was started under a diagnosis of probable DLB and donepezil therapy suppressed the visual hallucinations.

In 200X+1, the MMSE score was 19, showing marked improvement. The cube copying test also showed marked improvement. However, he still had pain and numbness of the lower abdomen, lower back, and bilateral lower limbs. He consulted the Department of Orthopedics, but no abnormalities were found. In the lower limbs, the pain only affected the dorsum of the foot and not the plantar region, excluding the possibility of diabetic polyneuropathy. Pregabalin was administered at 25 mg/day. Improvement of his pain was confirmed after several weeks and there has been no recurrence, although the observation period is still only a few months.

DISCUSSION

We used pregabalin to treat neuropathic pain (probably central pain) in 3 patients with LBD attending our outpatient clinic, and the pain responded well to administration of this drug at a low dose of 25 to 50 mg/day in all 3 patients.

We noted the following common points of these 3 patients :

1. A low dose of pregabalin (25 to 50 mg/day) was effective for pain that was probably related to degeneration of central neurons in LBD.
2. From one to three weeks was required until the effect of pregabalin on pain was noted.
3. No other analgesics were necessary as adjuvant care.
4. There were no adverse reactions of pregabalin in these 3 cases.
5. There was still no recurrence of the pain after it responded to pregabalin (follow-up periods of each case : 1 year and several months, about 6 months, and a few months).

Regarding the mechanism by which pregabalin acts on pain, it may bind to the $\alpha 2\delta$ subunit of the voltage-dependent calcium-channel, reducing calcium influx and the release of neurotransmitters such as glutamic acid.[11,12] However, the detailed mechanism remains to be clarified. In particular, the pharmacological mechanism involved in the efficacy of pregabalin for central neuropathic pain is unclear. An increase in spinal cord expression of the $\alpha 2\delta$ subunit was reported in a rat spinal cord injury model, suggesting that pregabalin could exhibit its analgesic action by inhibiting this

subunit.[12)]
Several clinical studies have indicated efficacy of pregabalin for central neuropathic pain, such as spinal cord injury-related pain and central pain after stroke.[9,10)] However, to our knowledge, there have been no previous reports on the efficacy of pregabalin for PD- or LBD-related central neuropathic pain.
In Japan, the standard dose of pregabalin for neuropathic pain is 300 to 600 mg/day, but the analgesic effect of pregabalin was satisfactory at much lower doses (25 to 50 mg/day) in our LBD patients. It has been reported that administration of pregabalin at 450 mg/day for diabetic polyneuropathy induced Parkinsonism, suggesting that deterioration of Parkinsonism should be considered when administering this drug to LBD patients.[13)] If low-dose pregabalin is effective, the results of treatment may be more favorable.
We have only treated 3 patients, and the follow-up period after onset of the analgesic effect of pregabalin is not long enough. In the future, a long-term study involving a larger number of patients should be conducted to better evaluate the efficacy and safety of low-dose pregabalin therapy for LBD-related central neuropathic pain. The risks in using pregabalin, such as syncope, fall, and hepatotoxicity were also considered as well as Parkinsonism.

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DISCLOSURE
None of the authors have any direct conflicts of interest relevant to this report.

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Possible effectiveness of low-dose pregabalin in a patient suffering from Lewy body disease and chronic pruritus

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Abstract
Many patients with Lewy body disease (LBD) complain of pain, although the detailed mechanism responsible for LBD-related pain remains to be clarified. On the other hand, to the best of my knowledge, there have not been any reports about LBD patients suffering from an itching sensation. In this report, I describe the case of an LBD patient who experienced severe itching that persisted for over 6 months, and report that low-dose pregabalin therapy was very effective against the patient's itching. This is the first study to report that low-dose pregabalin seemed effective against itching in a patient with LBD, as has been found for LBD-related pain.

INTRODUCTION
In patients with Lewy body disease (LBD), the central nervous system (CNS), including the motor, sensory, and autonomic nervous systems, is extensively affected. Therefore, pain related to the degeneration of the CNS is often observed. Such pain, a kind of central neuropathic pain, has recently become a focus of attention as a prodromal symptom of LBD. Although the efficacy of drug therapy against such pain has not been established, we have recently reported 3 cases in which suspected central neuropathic pain was successfully ameliorated in LBD patients using low-dose pregabalin.[1]
In the field of dermatology, chronic pruritus is a well-known condition.[2] It is defined as itching that persists for more than 6 weeks despite the absence of a skin lesion. It can involve the entire skin (generalized pruritus) or only particular areas, such as the scalp, upper back, and arms (localized pruritus). It frequently develops in middle-aged or elderly people. It is considered to be associated with other diseases, such as liver, kidney, hematological, and endocrine diseases, although its detailed etiology remains to be clarified. No treatment for such itching has yet been established, and there have only been a few case reports about the use of antidepressants or pregabalin to treat chronic pruritis.[3]
In this case, low-dose pregabalin was used to treat severe itching, which had persisted for over 6 months, in a patient with LBD. To the best of my knowledge, this is the first case report in which the administration of low-dose pregabalin seemed effective against chronic pruritus in a patient with LBD. This raises a question as to whether a relationship exists between LBD and chronic pruritus.

CASE REPORT
Written informed consent to present this report was obtained from the patient and his family. Minor modifications to the case details that did not affect the findings of this study were made to preserve the patient's anonymity.
The patient was a Japanese male in his early 80s. His medical history did not include any relevant conditions, except for recurrent nocturnal dream-enactment behavior from 200X-3. Since it became difficult for him to perform routine accounting tasks in 200X-2, he consulted the Department of Neurology at another hospital and was diagnosed with mild cognitive impairment. In 200X-1, he started to experience vivid visual hallucinations, e.g., of unknown individuals, and water on the floor, and he also complained of a reduced sense of smell, e.g., being unaware of the smell of fragrant orange-colored olives.
In 200X, the patient consulted my department. He complained of visual hallucinations; cognitive disturbances involving fluctuations in attention and alertness; severe itching on his head including both ears; and the abovementioned symptoms; i.e., rapid eye movement sleep behavior disorders and olfactory dysfunction. On examination, mild cogwheel-like rigidity of the right hand was observed, as well as impaired postural reflexes and parkinsonian gait. His Mini-Mental State Examination score was 21 points, which was indicative of severe constructional apraxia. Cranial magnetic resonance imaging did not reveal any abnormalities. Treatment with donepezil therapy was started under a diagnosis of probable dementia with Lewy bodies. Within about 5 months, donepezil had suppressed his visual hallucinations, but the itching persisted. Although he consulted a dermatology clinic, no abnormalities were found, and no treatment was administered.

Although the cause of his head itching was unclear, pregabalin was administered at a dose of 25 mg/day, after informed consent for its off-label use and the possibility of side effects had been obtained from him and his wife, based on a suspicion that his symptoms might be related to LBD-induced CNS degeneration. At the next consultation, the patient reported a marked reduction in the severity of his itching. In fact, he reported a marked improvement about 1 week after the start of the pregabalin therapy, stating that "The severity of the itching had decreased to a tolerable level, which I feel is about 30%", "I do not have to scratch my head", and "I do not wish to increase the dose of that drug (pregabalin)".
During the subsequent follow-up period (about 10 months), the itching did not deteriorate. The patient did not suffer any adverse reactions to the pregabalin treatment.

DISCUSSION

The patient described in this report had LBD and chronic pruritus. To the best of my knowledge, no previous studies have described this combination of conditions, possibly because clinicians have not paid enough attention to the concomitant development of LBD and pruritus. In the present case, it is possible that the concomitant development of LBD and pruritus was incidental. On the other hand, there is a possibility that the patient's head itching was related to CNS degeneration caused by his LBD.
The characteristics of this case are presented below :
(1) This is the first case report about chronic pruritus complicated with LBD.
(2) This patient had no other diseases except LBD.
(3) Low-dose pregabalin (25 mg/day) was administered based on the possibility that the patient's Lewy pathology might have contributed to the development of his chronic pruritus.
(4) Low-dose pregabalin therapy seemed markedly effective in this patient.
(5) It took about 1 week for the patient's itching to improve. These are consistent with the results of our previous report on LBD-related central neuropathic pain.[1]
The relationship between pain and itching sensations has been discussed in previous studies. Pain and itching share many common characteristics : they are both classified into peripheral and central sensations, peripheral pain/itching is transmitted to the upper sensory nervous system through the unmyelinated C fibers of primary afferent neurons, and descending modulatory control systems for pain/itching are present in the CNS. On the other hand, differences between the mechanisms responsible for the two sensations are also known to exist. For example, opioids, which reduce pain by binding to opioid receptors in the CNS, can induce itching sensations via μ-receptors.
Pain is clinically classified into 3 types based on its etiology : (1) nociceptive pain related to the stimulation of the free nerve endings of afferent neurons, (2) peripheral neuropathic pain (e.g., post-herpetic neuralgia, diabetic polyneuropathy), and (3) central neuropathic pain (e.g., spinal cord injury-related pain, LBD-related pain). Itching is classified in a similar manner : (1) dermatological itching related to the stimulation of the free nerve endings of afferent neurons; (2) neuropathic itching related to peripheral sensory nerve abnormalities (e.g., post-herpetic itching); and (3) itching with a systemic cause, in which opioid receptors in the CNS might be involved (e.g., cholestasis, chronic kidney disease).[2] During comparisons of these classifications, it becomes obvious that the pathogenesis of pain resembles that of itching; i.e., dermatological itching corresponds to nociceptive pain, and neuropathic itching corresponds to peripheral neuropathic pain. However, does itching caused by systemic factors correspond to central neuropathic pain?
Itching caused by systemic factors is associated with several systemic diseases, such as cholestasis and chronic kidney disease. The detailed mechanism responsible for such itching remains to be clarified; however, it might involve the binding of endogenous opioid peptides, such as β-endorphin, to μ-receptors in the CNS. Patients with cholestasis or chronic kidney disease exhibit higher serum levels of β -endorphin. On the other hand, no previous studies have described the pain sensation generated by systemic diseases. Therefore, there might not be an equivalent pain entity to itching caused by systemic factors.
If central neuropathic pain does not correspond to itching caused by systemic factors, then is there a type of itching that is equivalent to central neuropathic pain? We speculate that such a condition might actually exist. For example, LBD might also induce so-called "central neuropathic itching" as well as central neuropathic pain. In addition to LBD, other neurodegenerative diseases that cause extensive disturbances of the CNS could also induce the same condition.
Although the detailed mechanism of action of pregabalin against neuropathic pain remains unclear, it is suggested that its effects are mediated by the descending modulatory control system in the CNS.[4] Similarly, as descending modulatory control systems for both itching and pain sensation are known to exist, the mechanism of action of pregabalin against itching might be similar to its mechanism of action against pain.[5]
Only a few reports have described the efficacy of pregabalin against itching, although there are no data from studies involving controls.[2,3] Thus, more case reports and data from studies involving controls are required. Furthermore, more case reports about LBD combined with chronic pruritus are needed in order to investigate both the possible relationship between LBD and chronic pruritus, and the efficacy of low-dose pregabalin against chronic pruritus derived from LBD.

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DISCLOSURE

None

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Transient epileptic amnesia without epileptic seizures : Proposal of a new entity

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CASE STUDY

A male in his early 60s attended our memory clinic with his wife. He said that his memory had become faulty about 4 years earlier, and he had experienced a lot of problems because of his forgetfulness. He had consulted other memory clinics, but no abnormalities had been found. He also stated that he had forgotten many events, such as traveling with his wife a few months earlier, having a colon polypectomy at another hospital about 2 years earlier, and the wedding ceremony of his daughter about 11 years earlier.
His Mini-Mental State Examination score was 29, and he could correctly recall a sentence that he had been asked to memorize about 30 minutes earlier. The patient seemed to be suffering from a disturbance of his long-term memory, but not his short-term memory, which affected his recall of events from several weeks, months, and years earlier. Although he had not exhibited any symptoms of epileptic seizures, electroencephalography was performed, and sharp waves were detected. The administration of levetiracetam was commenced, and the dose was increased to 1500 mg/day, resulting in an improvement in the patient's anterograde amnesia. He was diagnosed with transient epileptic amnesia (TEA) involving accelerated long-term forgetting (ALF) and autobiographical amnesia. However, he did not believe that he had suffered any amnesia attacks, and his wife, daughter, and friends agreed with this.
Several years after the start of the levetiracetam therapy, he did not display any abnormal symptoms and was able to work without any difficulty.

DISCUSSION

TEA is a special type of epilepsy.[1-4] Zeman et al. developed the following diagnostic criteria for the condition : (1) recurrent, witnessed episodes of amnesia; (2) other cognitive functions remain intact during attacks; and (3) evidence of epilepsy. In addition, they noted that patients with TEA almost always exhibited 2 other types of memory symptoms : ALF (the unexpected and rapid disappearance of memories of events that occurred in recent days, weeks, or months) and autobiographical amnesia (the discovery of large gaps in more remote autobiographical memories). Thus, TEA causes 3 characteristic memory symptoms.

To make a diagnosis of epilepsy, the presence of epileptic seizures is required. However, the patient described in this report did not exhibit any clinical symptoms of epileptic seizures, including amnesia attacks. The key characteristics of this case are outlined below :

1. According to the definition of epilepsy, our patient could not be diagnosed with epilepsy.
2. According to Zeman's diagnostic criteria, our patient could not be diagnosed with TEA.
3. Abnormal neuronal discharges without clinical seizures (so-called "subclinical seizures") might cause both ALF and autobiographical amnesia because levetiracetam improved both of these symptoms in the present case.

Should our patient have been diagnosed with epilepsy? If TEA is ruled out, what term should be used for our patient's disease?

To overcome these problems, we offer the following suggestions :

1. Patients that meet all of Zeman's criteria should be regarded as having TEA.
2. Patients that do not experience amnesia attacks despite suffering from ALF and/or autobiographical amnesia should be considered to be suffering from "broad TEA".
3. Conditions such as that seen in the present case must have an epileptic mechanism, and so they should be diagnosed as epilepsy.

It would be inconsistent to regard patients without amnesia attacks as having TEA, but the existence of "broad TEA" suggests that transient amnesia attacks are caused by the same pathogenic mechanism as ALF and/or autobiographical amnesia. In other words, abnormal neuronal discharges can cause not only transient amnesia attacks, but also ALF, which might be associated with a failure of memory consolidation (maybe taking several weeks or months), and autobiographical amnesia, which might be due to the disruption of consolidated remote memories (maybe taking several years). "Subclinical seizures" might be responsible for broad TEA.

One or more clinical epileptic seizures are required for a diagnosis of epilepsy. Therefore, patients with ALF and/or autobiographical amnesia in the absence of amnesia attacks cannot be diagnosed with epilepsy. However, it is certain that an epileptic mechanism (i.e., an abnormally excessive neuronal discharge) is involved in the etiology of both ALF and autobiographical amnesia. Therefore, it might be appropriate to regard patients with broad TEA as having epilepsy, regardless of the presence or absence of amnesia attacks.[5]

DISCLOSURES

None

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日本における石灰沈着を伴うびまん性神経原線維変化病（小阪・柴山病）

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石灰沈着を伴うびまん性神経原線維変化病（DNTC）は、おもに初老期に発症する稀な認知症性神経変性疾患の一つである。日本以外の国での報告が極めて少ないのは、この疾患に関する認識が不充分であるため、見逃されている場合が多いのであろうと推測される。日本における DNTC の報告例を総括し、その臨床病理学的特徴と問題点を明らかとし、さらに新たな臨床診断基準を提唱する。

＜検索用語：石灰沈着を伴うびまん性神経原線維変化病（DNTC）、小阪・柴山病、Fahr病、特発性基底核石灰化症、臨床診断基準＞

【はじめに】

「石灰沈着を伴うびまん性神経原線維変化病（diffuse neurofibrillary tangles with calcification; DNTC）」の世界初の症例報告論文は、名古屋大学精神医学教室の小阪憲司らによって発表された[27]。小阪の共同研究者であった柴山漠人らは3剖検例からなる最初の英語論文を発表した[51]。のちに柴山らはこの疾患に対して "non-Alzheimer non-Pick dementia with Fahr's syndrome" という病名を提唱したが[52]、現在一般的な呼称となった DNTC という病名は小阪が提唱したものである[29]。これらの業績から、この疾患は欧米では "Kosaka-Shibayama disease" とも呼ばれる。この疾患の臨床病理学的特徴は、① Alzheimer病（AD）と Pick病（PiD）の特徴を併せ持った進行性の認知症、② Fahr病と類似した顕著な脳内石灰沈着、③側頭葉の著明な萎縮とグリオーシス、④多数の神経原線維変化（neurofibrillary tangle; NFT）の出現、⑤老人斑の欠如、などである[29,52]。

【研究の方法および結果】

1.　対象と方法

PubMed, Medline, JDREAM III、および医学中央雑誌を用いて、DNTC に関するすべての論文を検索した（2012年中頃まで）。これらの論文を詳細に検討した結果、剖検例は28例（本邦26例）、臨床診断症例は23例（本邦21例）であった。そのほかに、これらの症例を用いての多数の臨床神経病理学的・画像研究報告や総説があった。

2.　結果

1）　我が国における DNTC剖検報告26例[68]

初発年齢は平均54.3（42-77）歳、死亡時年齢は平均66.5（48-79歳）、罹病期間は平均10.1（2-30）年であった。男女比は、1：2.7（7：19）で女性に多く、家族発症が確認された例はなかった。もっとも多かった初発症状は、AD と同様に記憶障害であった。その一方、常同行為、性格変化、脱抑制、考え不精など、PiD類似の症状も認められた。臨床診断名は、AD（6例）、PiD（5例）、初老期痴呆（5例）、老年期精神病（2例）、DNTC（1例）であった（未記載7例）。

平均脳重量は995.2（720-1265）g であった。PiD類似の限局性側頭葉萎縮が特徴的であり、萎縮した部位には、AD と同様に多数の NFT の出現を認めた。老人班はほとんど認められず、被殻・淡蒼球・小脳歯状核などに左右対称の著明な石灰化が認められた。

2）我が国における DNTC臨床報告21例[68]

初発年齢は平均64.6（47-82）歳、男女比は、1：5.7（3：17、未記載1）で女性に多く、家族発症例はなかった。臨床症状としては、上記に加え、幻覚、妄想、暴力、パーキンソン症状、ジスキネジアなど、多彩な精神運動症状が認められた。

【考察】

1.　神経病理学的特徴

1）側頭葉萎縮

限局的な側頭（前頭）葉萎縮は DNTC の最も特徴的な所見の一つであり、この点からは DNTC は前頭側頭葉変性症に分類されるといえる。萎縮部位の白質は、顕著な脱髄とグリオーシスを伴っている。Kosaka は、DNTC では PiD とは異なり上側頭回や海馬も強く萎縮するとしたが、Tsuchiya らは、上側頭回は比較的保たれると述べている[64]。

2）NFT

Ukai らは、DNTC における NFT の分布は AD に類似しているが、側頭葉では側頭極に近いほどその密度が増え、細胞外の NFT（いわゆる ghost tangles）も多いことを指摘した[67]。Tanabe らは、生化学的・免疫組織学的に検討し、DNTC の NFT は AD と同様であり、3リピートおよび4リピートタウからなることを見出した[60]。

3）Fahr型の脳内石灰沈着

DNTC の脳内石灰沈着の病態や特発性基底核石灰化症（IBGC）との関連などは不明である。IBGC には家族性の症例も多く、いくつもの原因遺伝子座が報告されている（詳細は省略。Nunomura論文参照）[47]。これに対し、家族性の DNTC は未だ報告されていない。また、DNTC は、進行性の認知機能低下、限局性側頭葉萎縮、タウ病理などで、IBGC とは区別

される。
Haraguchi らは、他疾患と比べて高濃度の鉛蓄積を特徴的と指摘したが[7,8]、これを否定する報告もある[11,12]。
4）その他
① グリア細胞の原線維変化（glial fibrillary tangle; GFT）
GFT は形態的に、thorn-shaped astrocyte、tuft-shaped astrocyte、coiled bodies の3種類に分類される。このうち、tuft-shaped astrocyte は進行性核上性麻痺に特徴的とされるが、Hashimoto らは DNTC でも見出されることを報告した[9]。
② α - シヌクレイン
ほとんどの症例でα - シヌクレインの異常蓄積が認められている[6,10,72]。しかし、その分布は、レビー小体病とは異なり、NFT と相関している。また、Iwasaki らは比較的早期の DNTC剖検例でα - シヌクレインの蓄積が認められなかったことから、DNTC ではα - シヌクレインの蓄積は遅い段階で始まると推測している[22]。
③ TAR DNA-binding protein of 43 kDa（TDP-43）
Habuchi らは、ほとんどの症例で TDP-43の異常蓄積が認められ、その分布は NFT と相関していることを報告した[6]。以上から、タウ、α - シヌクレイン、TDP-43の間の関連性が示唆され、その解明が待たれる。
④ Plaque-like structure（PLS）
Terada らは、DNTC のみに出現する血管周囲の構造物を見出し、PLS と名付けて報告した[62]。この構造物は、コラーゲン線維やタウとも異なり、その主成分は現在のところ不明である。

2. 診断マーカー
1）脳血流 SPECT
側頭前頭葉に強い血流低下を認める（FDG-PET では側頭前頭葉の糖代謝低下が報告されている）[15,18,19,50]。その一方、石灰化の強い大脳基底核や小脳では意見の一致を見ていない。
2）髄液検査
髄液検査の報告は少なく、未だに意見の一致を見ていない[18,49,69]。

3. DNTC の臨床診断基準
1）新しい DNTC の臨床診断基準の提案
DNTC の臨床診断基準は、岩井・柴山のグループによって[21]、さらに小阪によっても提案されている[31]。しかし、これらの臨床診断基準は、DNTC の臨床的特徴を列記しただけであった。そこで今回、改めて DNTC 剖検報告を検討して、新しい臨床診断基準案を作成した[68]。
この臨床診断基準は、一つの必須な特徴（認知機能低下）、三つの中核的特徴（① Fahr型の脳内石灰沈着、②側頭葉・前頭葉症候群、③両側性の限局性側頭葉萎縮）、および六つの支持的特徴からなり、probable DNTC と診断するためには、Fahr型の脳内石灰沈着と側頭葉・前頭葉症候群、または Fahr型の脳内石灰沈着と限局性側頭葉萎縮を満たす必要があるとした。Possible DNTC と診断するためには、Fahr型の脳内石灰沈着を認めるのみでよい。
FDG-PET や髄液検査所見は未だ報告数が少ないため、将来の課題とした。
2）新しい臨床診断基準案について
新しい臨床診断基準の三つの中核的特徴のうち、Fahr型脳内石灰沈着と両側性限局性側頭葉萎縮は、頭部 CT（または MRI）画像によって診断されることになる。ところで、DNTC剖検報告26例のうち、頭部 CT が実施され・その所見が記載されたものは9例に過ぎない[4,20,23,36,39,51,58,66]。この9例全例で、限局性側頭葉萎縮の画像所見が記載されていた。一方、この9例のうち、側頭葉・前頭葉症候群の臨床症状所見が明確に記載されていたものは4例であった[23,51,58]。この臨床診断基準の感度・特異度はともに未検証であり、今後検証されるべき課題である。

4. 早期 DNTC剖検例
世界の DNTC剖検例28例のうち、2例が早期の DNTC症例であった。Kosaka らは、軽度の記憶障害を認めた70歳女性の剖検報告で、海馬・海馬傍回・扁桃核に多数の NFT を認めたと記載している[30]。また、Langlois らは、64歳女性の剖検例を報告し、海馬・海馬傍回に多数の NFT を認めたと記載している[35]。わずか2例からの推測であるが、DNTC のタウ病理は AD と同様に、海馬・海馬傍回・扁桃核から始まるのであろうと思われる。

5. DNTC は日本に多いのか？
報告された DNTC症例のほとんどが、我が国の症例である理由は不明である。一つの可能性として、欧米では、DNTC症例が Fahr病として報告されているのかもしれない。例えば、Avrahami らは、32例の Fahr病患者のうち、15例に認知症が認められたと報告している[1]。この15症例のなかに、DNTC が含まれている可能性がある。一方、NFT が認められない Fahr病の剖検報告も多数存在する。おそらく、DNTC や前述した家族性 IBGC以外にも、Fahr病にはいくつかの疾患が含まれているのであろう。

6. 本論文の意義、苦労した点など
DNTC の総説は、これまでにもいくつか発表されている。例えば、1992年の小阪[28]、1994年の柴山[53]、1996年の竹内・柴山[59]、1997年の Kosaka[32]、2001年の田辺・黒田[61]、2006年の横田ら[73]、2010年の Kuroda et al.[34]、2011年の藁谷[70]、による総説などである（著者らの後に発表された総説としては、2016年の寺田による優れた総説があり[63]、これには2015年までの文献による新知見が加えられている）。また、DNTC の優れた臨床診断基準としては、前述した岩井・柴山らによるものがある[21]。この状況で著者らが新たな総説を記したのは、欧米では DNTC の知名度が未だに低いことが大きい。これまでの DNTC の臨床診断基準が日本語で書かれていたこともあり、英文で新しい診断基準案を作成した。欧米での DNTC への注目がより高まり、その結果、症例報告が多数発表されることを期待している。
苦労した点は、症例を集めるにあたり、現在では DNTC と一般的に呼ばれるこの疾患には、別名・類似疾患名での報告が多かったことがある。例えば、Fahr病、非定型初老期痴呆、脳内石灰化症、などである。また、まれな疾患であるため、一つの症例がいろいろな視点から検討されて複数の論文に繰り返し用いられていることが多く、症例の異同の判定には苦労をした。よって、著者らが誤認・見過ごしている症例もあるかもしれないので、忌憚のないご指摘をいただけたら幸いである（著者らが認識できたすべての症例を、文献に載せてある[68]）。

【展望】
DNTC患者脳の生化学的な検討は、ほとんどなされていない。例えば、DNTC ではマイネルト基底核の障害も大きいので、脳内アセチルコリン濃度は AD と同様に低下しているだろうと推定することはできるが、実証はされていない。また、上述した様々な神経病理学的所見や診断マーカー、例えば、PLS や tuft-shaped astrocyte、α- シヌクレインや TDP-43の生成分布過程、脳脊髄液中のタウ蛋白、FDG-PET所見、大脳基底核や小脳の血流低下の有無なども、さらに調査・検討されるべきである。これらの問題が解決された暁には、著者らが提案した新しい臨床診断基準も、さらなる改訂が必要となろう。

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Relationship between the Contrast Enhancement of the Perivascular Space in the Basal Ganglia with Endolymphatic Hydrops

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Purpose : We routinely obtain the endolymphatic hydrops (EH) image using heavily T2-weighted 3D-FLAIR (hT2w-3D-FLAIR) imaging at 4 hours after intravenous administration of a single-dose of gadolinium-based contrast media (IV-SD-GBCM). While repeating the examination, we speculated that the contrast enhancement of the perivascular space (PVS) in the basal ganglia might be related to the degree of EH. Therefore, the purpose of this study was to investigate the relationship between the endolymphatic volume ratio ($\%EL_{volume}$) and the signal intensity of the PVS (SI-PVS).
Materials and Methods : In 20 patients with a suspicion of EH, a heavily T2-weighted 3D-turbo spin echo sequence for MR cisternography (MRC) and an hT2w-3D-FLAIR as a positive perilymph image (PPI) were obtained at 4 hours after IV-SD-GBCM. The $\%EL_{volume}$ of the cochlea and the vestibule were measured on the previously reported HYDROPS2-Mi2 image. The PVS in the basal ganglia was segmented on MRC using a region-growing method. The PVS regions were copied and pasted onto the PPI, and the SI-PVS was measured. The larger value of the right and the left ears was employed as the $\%EL_{volume}$, and the weighted average of both sides was employed as the SI-PVS. The correlation between the $\%EL_{volume}$ and the SI-PVS was evaluated.
Result : There was a strong negative linear correlation between the $\%EL_{volume}$ of the cochlea and the SI-PVS ($r = -0.743$, $P < 0.001$); however, there was no significant correlation between the $\%EL_{volume}$ of the vestibule and the SI-PVS ($r = -0.267$, $P = 0.256$).
Conclusion : There was a strong negative correlation between the cochlear $\%EL_{volume}$ and the SI-PVS. Contrast enhancement of PVS might be a biomarker of EH.

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Decreased grip strength, muscle pain and atrophy occur in rats following long-term exposure to excessive repetitive motion

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Abstract :
Work-related musculoskeletal disorders (WMSD) are caused by the overuse of muscles in the workplace. Performing repetitive tasks is a primary risk factor for the development of WMSD. Many workers in highly repetitive jobs exhibit muscle pain and decline in handgrip strength, yet the mechanisms underlying these dysfunctions are poorly understood. In our study, rats performed voluntary repetitive reaching and grasping tasks (Task Group), while Control group rats did not perform these activities. In the Task Group, grip strength and forearm flexor withdrawal threshold declined significantly from week 2 to week 6, compared with these values at week 0 ($P < 0.05$). Relative muscle weight and muscle fiber cross-sectional area of flexor digitorum superficialis (FDS) muscles decreased significantly in the Task group, compared with the Control group, at 6 weeks ($P < 0.05$ and $P < 0.01$, respectively). Nerve growth factor, glial cell line-derived neurotrophic factor and tumor necrosis factor α expression in FDS muscles was not significantly different in Control and Task groups at 3 and 6 weeks. At 6 weeks, the Task group had elevated MuRF1 protein levels ($P = 0.065$) and significant overexpression of the autophagy-related (Atg) proteins, Beclin1 and Atg5–Atg12, compared with in the Control group (both $P < 0.05$). These data suggested that long-term exposure to excessive repetitive motion causes loss of grip strength, muscle pain and skeletal muscle atrophy. Furthermore, this exposure may enhance protein degradation through both the ubiquitin-proteasome and autophagy-lysosome systems, thereby decreasing skeletal muscle mass.

Keywords :
work-related musculoskeletal disorders; grip strength; muscle pain; muscle atrophy; ubiquitin-proteasome system; autophagy-lysosome system

Abbreviations :
WMSD, work-related musculoskeletal disorders; TNF, tumor necrosis factor; IL, interleukin; DOMS, delayed-onset muscle soreness; NGF, nerve growth factor; GDNF, glial cell line-derived neurotrophic factor; CSA, cross-sectional area; MuRF1, muscle RING finger 1; Atrogin-1, muscle atrophy F-box/Atrogin-1, Atg, autophagy-related; LC3, microtubule-associated protein 1 light chain 3; FDS, flexor digitorum superficialis; qRT-PCR, quantitative reverse transcription PCR; SDS-PAGE, sodium dodecyl sulfate-polyacrylamide gel electrophoresis; PVDF, polyvinylidine difluoride; CBB, Coomassie Brilliant Blue; ELISA, enzyme-linked immunosorbent assay; SEM, standard error of the mean; ANOVA, analysis of variance; EDL, extensor digitorum longus

Running heading :
Muscle dysfunction caused by repetitive tasks

Introduction :
Work-related musculoskeletal disorders (WMSD) are defined as injuries or musculoskeletal effects caused by exposure to certain risk factors in the workplace. Risk factors for WMSD include repetition, force and awkward or static postures. Previous research showed that in highly repetitive jobs (a cycle time less than 30 s or more than 50% of the time performing same type of fundamental cycle), there was a 2.8 odds ratio of injury compared with in low repetition jobs [1]. Of female workers in highly repetitive jobs, 23% reported muscle pain in forearm and hand muscles [1]. Furthermore, women seeking medical care for WMSD of the upper extremities also showed decreased handgrip strength, and these symptoms were related to their levels of perceived physical exertion [2].
Using rat models, previous studies have investigated the pathophysiology of injuries of the upper forelimb caused by voluntary repetitive reaching and grasping tasks [3, 4]. Several investigators reported that the repetitive tasks caused decreased grip strength [5–9]. Barbe *et al.* reported that performance of voluntary repetitive reaching and grasping tasks led to increased levels of tumor necrosis factor (TNF)-α, interleukin (IL)-1α and IL-1β in rat forearm flexor muscles [5]. Furthermore, this task led to elevated levels of substance P and its preferred receptor, neurokinin-1, in the spinal cord dorsal horn [10]. In addition, previous studies showed that high repetition tasks increased fibrogenic-related proteins in skeletal muscle or tendon [7–9].

Several inflammatory cytokines, including TNF-α IL-1α, IL-1β were implicated in pain. Substance P is another major mediator of neuropathic inflammatory pain. Therefore, muscle pain would be expected to occur in volunteers performing repetitive reaching and grasping tasks. Recently, Xin *et al*. [11] studied skin pain, often assessed with a von Frey hair test, in a WMSD model. However, according to Nasu *et al*. [12], it is necessary to use a probe with a diameter of at least 2.6 mm to evaluate the mechanical threshold of skeletal muscle. Thus, while factors affecting decreased grip strength after repetitive reaching and grasping tasks have been proposed in several studies [5–9], those affecting pain in such models have not been identified. It remains to be demonstrated that a rat model for repetitive tasks exhibits similar muscle pain as that seen in workers with highly repetitive jobs.

In several other animal models, muscle pain was produced by exercise stresses different from the repetitive reaching and grasping tasks. Some animals were forced to exercise by repetition of eccentric contractions. After such exercise, they experienced delayed-onset muscle soreness (DOMS) and declines in mechanical withdrawal threshold in the muscle [13, 14]. In a previous study, physical exercise, including eccentric contractions, induced expression of nerve growth factor (NGF), glial cell line-derived neurotrophic factor (GDNF) and TNF-α in skeletal muscle and, consequently, led to decreased muscle mechanical thresholds [13, 15, 16]. NGF, produced in skeletal muscle after ischemia [17] or nerve injury, can sensitize muscle nociceptors [18]. Like NGF, GDNF is also responsible for growth and maintenance of certain neurons. In rats, injection of either NGF or GDNF into skeletal muscle led to a decline in the mechanical threshold [16, 19]. Therefore, we hypothesized that performance of repetitive reaching and grasping tasks by rats would lead to upregulation of NGF, GDNF and TNF-α and to declines in mechanical thresholds in muscle.

It is further worth noting that generally, pain reduces muscle strength [20–22]. However, studies showed strong correlations between muscle force and either muscle volume or cross-sectional area (CSA) [23–25]. Hence, not only muscle pain, but also skeletal muscle atrophy, may be responsible for the decline in grip strength caused by repetitive reaching and grasping tasks. Changes in skeletal muscle mass, in rats performing the tasks, have not been investigated.

Skeletal muscle adaptation depends on dynamic interplay between changes in muscle protein synthesis and degradation. Both the ubiquitin-proteasome and autophagy-lysosome systems are involved in degradation of skeletal muscle proteins.

The ubiquitin-proteasome system degrades soluble and myofibrillar proteins [26]. Specificity of substrate tagging is ensured by ubiquitin ligases. For example, levels of two muscle-specific ligases, muscle RING finger 1 (MuRF1) and muscle atrophy F-box/Atrogin-1 (Atrogin-1), were increased in several instances of catabolism [27]. MuRF1 and Atrogin-1 are believed to selectively bind substrates for ubiquitination and subsequent degradation by the 26S proteasome. Thus, increased MuRF1 and Atrogin-1 expression following an atrophy-inducing stressor is attributed to the shift in protein balance from net synthesis to net degradation [28]. The process of autophagy begins with autophagosome formation, in which a double membrane is formed around a portion of the cytoplasm containing proteins and/or organelles. Autophagosome formation is under the control of proteins encoded by autophagy-related (Atg) genes. In particular, two ubiquitin-like conjugation systems were described. In the first, the Atg5–Atg12 complex can interact with Atg16 to participate in autophagosome membrane formation. The second involves Atg8, also known in mammals as microtubule-associated protein 1 light chain 3 (LC3) . LC3II was implicated in substrate selection for degradation and in membrane fusion and, when bound to phospholipid, is known as LC3II [29]. Among proteins implicated in control of the autophagy process, the Atg6 homolog Beclin1 appears to be central for initiation of sequestration [30. 31].

In one report, long-term running exercise led to increased MuRF1 protein expression and proteasome activity [32] and increased levels of Atg proteins Beclin1 and LC3II, suggesting increased basal autophagy [33], in plantaris muscle of mice. Thus, long-term running exercise is believed to promote muscle protein degradation through these two systems. However, changes, during repetitive reaching and grasping tasks, in molecules involved in muscle protein degradation were not yet investigated.

Therefore, the first purpose of our study was to investigate factors involved in decreased grip strength, from the perspective of muscle pain and skeletal muscle mass, associated with voluntary repetitive reaching and grasping tasks in the rat. The second purpose was to examine key regulators of muscle pain associated with the task. The third purpose was to evaluate repetitive task-dependent activation of the ubiquitin-proteasome and autophagy-lysosome systems. In this study, we chose a rat model not involving use of force. As shown by Barbe *et al*. [5] and Clark *et al*. [6], rats performing continued repetitive reaching and grasping tasks (high repetition negligible force model) exhibited dysfunctions similar to those in humans. This indicated that high frequency motion, not necessarily involving high force, induces WMSD. Thus, in our study, we investigated the hypothesis that long-term exposure to excessive repetitive motion would cause loss of grip strength, muscle pain and skeletal muscle atrophy and, furthermore, that such atrophy would involve enhanced protein degradation through the ubiquitin-proteasome and autophagy-lysosome systems.

Materials and Methods :

Animals

All animal procedures were performed under the animal care guidelines of Nagoya University. A total of 41 female Sprague-Dawley rats, aged 10 weeks, were used for this study. Rats were from Japan SLC (Hamamatsu, Japan) and were housed under controlled temperature (25℃) and lighting (8 : 00–20 : 00 light) conditions. Rats were divided randomly into food-restricted control (Control, n = 19) or task (Task, n = 22) groups. Control and Task groups were restricted from food for 5 or 8 weeks. These rats were food deprived so that they maintained 80%–90% of full body weight, as defined by the weights of age-matched normally fed rats. Rats were weighed weekly and their food adjusted accordingly [3, 4, 6]. After a 2 week training period (described below) and the first 3 weeks of the Task period (this time is known as "3 weeks" in our study) , the rats in each group were further subdivided to perform certain analyses. The reason was to avoid potential artifacts in the muscle tissue analyses introduced by prior behavioral testing. Thus, a subset of the Control group at 3 weeks (n = 6) and Task group at 3 weeks (n = 6) were never subjected to behavioral analysis. This enabled their muscle samples to be used for both histological (*i.e*., measurements of relative muscle weight and muscle fiber CSA) and molecular biological and biochemical (*i.e*., mRNA expression relevant to muscle pain, ubiquitin-proteasomes and autophagy-lysosomes) analyses because these rats had no potential effects of behavioral analysis. For rats providing tissue at the 6 week time point, the type of behavioral testing they'd been subjected to determined which types of analyses could be performed on their tissues. Thus, behavioral analysis data (grip strength and pain) were examined only in certain rats and these were measured for the 6 consecutive weeks of the Task period (*i.e*., the Control group, in which grip strength was measured (n = 6), the Control group, in which muscle pain was measured (n = 7), the Task group at, in which grip strength was measured (n = 6), and the Task group in which muscle pain was measured (n = 10)). Grip strength and pain were performed on separate groups of rats but, for each parameter, the same rats were compared each week. For the "week 6" tissue samples, histological analysis (*i.e*., measurements of relative muscle weight and muscle fiber CSA) and molecular biological and biochemical analyses (*i.e*., mRNA and protein expression relevant to ubiquitin-proteasomes and autophagy-lysosomes) were performed using muscle tissue from rats in which grip strength had been measured. In contrast, NGF, GDNF and TNF-α levels were measured using muscle tissue from rats in which muscle pain had been measured. The reason for this was the concern that applying mechanical stimulation to the skeletal muscle, necessary to measure muscle pain, would affect skeletal muscle size. For example, in previous studies, skeletal muscle atrophy was suppressed by mechanical stimulation such as stretching [34, 35]. Therefore, we did not want to analyze skeletal muscle size in rats that had been tested for pain. It should be noted that the body weights did not differ between the Control and Task groups throughout the experimental period. Thus, differences in muscle, such as fat content, caused by excessive weight would not have confounded our histological analyses.

Voluntary repetitive reaching and grasping tasks

Rats were placed in the test box, as described by Metz and Whishaw [36]. There was a 1.3 cm wide vertical opening in the middle of the front wall enabling rats to reach for pellets placed on a shelf. Food pellets (45mg, BioServ, Frenchtown, NJ, USA) were dispensed every 15 s during the task. The rats voluntary performed the repetitive reaching and grasping tasks to obtain food pellets (Fig. 1). When a rat appeared likely to react to the pellets, an observer played a sound that was timed with pellet distribution [3, 4]. In addition, the observer adjusted the position of the pellet, so that the rats could grip the pellet with only one paw at a time. Control and Task groups were initially trained for 2

weeks to learn the voluntary repetitive reaching and grasping task for obtaining a food pellet. After the initial training period, only the Task group rats performed the repetitive reaching and grasping tasks, for 2 h/day, 3 days/week, for 3 or 6 consecutive weeks. An observer counted the number of reaches and grasps, how many food pellets were obtained and task durations. The task duration was defined as the total time that the rat participated in the task, and was as long as 2 h/day. These task parameters were used as the indicators of physical load. As previously described [3], this model used a "high repetition, negligible force" task.

Forelimb grip strength measurement
Rats were lifted by the tail and induced to grasp a rigid bar attached to a digital force gauge (Aikoh Engineering Corporation, Osaka, Japan). Each rat was gently pulled backward by the tail and the tension reading of the digital force gauge, just before the rat released the bar, was defined as grip strength. The test was performed 5 consecutive times and the highest value from the 5 trials was recorded as the grip strength.

Withdrawal threshold measurement
Muscular mechanical hyperalgesia was measured as a forearm withdrawal threshold, in response to gradually increasing mechanical forces applied to the forearm flexors (flexor digitorum superficialis (FDS) muscle included). The method was a modification of that described by Nakano et al. [37] (Fig. 2). Briefly, the head and trunk of the rat were wrapped with a cloth and the rat was suspended in a homemade hammock. We confirmed that, under these conditions, the forelimb position was freely movable. Forearm withdrawal threshold was quantified with a Pressure Application Measurement device (Ugo Basile, Comerio, Italy) equipped with a handmade round-headed probe (5 mm tip diameter) . It has been previously shown that a probe with a tip diameter of 5 mm allows measurements of the muscle mechanical nociceptive threshold [12]. The pressure required to elicit forelimb withdrawal was determined and measurements were taken 5 times at 1 min intervals. The mean value of these measurements was used as the forearm flexor withdrawal threshold.

Tissue collection
Tissues were collected from a total of 34 rats, from the Control group at 3 weeks (n = 6) and 6 weeks (n = 11) and from the Task group at 3 weeks (n = 6) and 6 weeks (n = 11). This tissue collection was performed 24–36 h after completion of the final task, to ensure that measurements reflected the chronic effects of long-term exposure to repetitive motion, rather than immediate effects of the last exercise. Similarly, in a previous study [5], muscle tissue was collected 18–36 h after the final task. Rats were euthanized by pentobarbital overdose (Nembutol; 120 mg/kg). FDS muscle from each reaching limb was harvested immediately after euthanasia. After harvesting, each muscle sample was cut into two pieces and these saved, respectively, for molecular biological and biochemical analyses and histological analysis. Specifically, muscles were cut across the midbelly portion and the distal part was used for molecular biological and biochemical analyses. The proximal part was used for histological analysis. We cut from the midbelly portion of the muscle to measure the CSA at the site where the muscle fiber became thickest [38, 39]. Muscle samples were flash frozen and stored at −80 ℃ until analyzed.

Morphological analysis of FDS muscles
A total of 24 frozen muscle samples were analyzed, from the Control group at 3 weeks (n = 6) and 6 weeks (n = 6) and from the Task group at 3 weeks (n = 6) and 6 weeks (n = 6). These samples were embedded in optimal cutting temperature compound (Sakura Fintek, Torrance, CA, USA), and cross sections (8 μm) were cut with a cryostat (CM1510S, Leica, Wetzlar, Germany) . These muscle cryosections were stained with hematoxylin and eosin (H&E) and images of the stained samples obtained with an optical microscope (BZ-9000, KEYENCE, Osaka, Japan) . Muscle fiber CSAs were measured from captured images using Image J software (National Institutes of Health, Bethesda, MD, USA) . Analysis was performed on at least 200 muscle fibers per muscle and these values were averaged.

RNA isolation
Muscles were homogenized in ice-cold Trizol Reagent (Invitrogen, Carlsbad, CA, USA) according to the manufacturer's instructions. After incubation for 5 min at room temperature, the mixture was centrifuged at 15,000 g for 10 min at 4 ℃ . The supernatant was transferred to a tube, a 1/5 volume of chloroform was added and sample was mixed. The mixture was incubated for 5 min at room temperature, then centrifuged at 15,000 g for 10 min at 4℃ . The aqueous layer was transferred to another tube and mixed with 0.8 volume isopropanol by pipetting. The mixture was incubated for 10 min at room temperature, then centrifuged at 15,000 g for 10 min at 4℃ . The RNA pellet was washed with 70% ethanol and centrifuged at 15,000 g for 10 min at 4℃ . RNA was dissolved in 20 μl RNase-free water with RNase inhibitor (final concentration 2 μg/μl) and further subjected to DNase treatment and reverse transcription using a ReverTra Ace qPCR RT Master Mix (Toyobo, Osaka, Japan).

Real-time quantitative reverse transcription PCR
Quantitation of gene expression was determined by real-time quantitative reverse transcription PCR (qRT-PCR). qRT-PCR reactions contained 2 μl cDNA, 10 μl TaqMan® Fast Advanced Master Mix (Life Technologies, Carlsbad, CA, USA) and 1 μl primers. The PCR reaction analysis was performed with a StepOnePlus Real-Time PCR system (Applied Biosystems, Foster City, CA, USA), using the ΔΔ Ct method. The primers were : NGF (Ngf, Rn01533872_m1), GDNF (Gdnf, Rn00569510_m1), MuRF1 (Trim63, Rn00590197_m1), Atrogin-1 (Fbxo32, Rn00591730_m1) , Beclin1 (Becn1, Rn00586976_m1) , Atg5 (Atg5, Rn01767063_m1), LC3 (Anxa3, Rn00563181_m1) and β-actin (Actb, Rn00667869_m1), all from TaqMan Gene Expression Assays (Life Technologies). β-Actin was used as an endogenous control to normalize results for each sample.

Protein isolation
Frozen muscle samples were homogenized in RIPA buffer plus 10% protease inhibitor cocktail (1 mg protein/10 ml RIPA), tissue lysates were centrifuged at 14,000 g for 10 min and the supernatants collected. Total protein was determined using the BCA-200 protein assay kit (Pierce, Rockford, IL, USA).

Western blot analysis
After measuring total protein content, each extract was adjusted to a concentration of 2 μg/μl with an appropriate volume of RIPA buffer for sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE). Lysates were mixed with equal volumes of EzApply (Atto, Tokyo, Japan) containing 100 mM Tris-HCl buffer (pH 8.8), 2% SDS, 20% sucrose, 0.06% bromophenol blue and 100 mM DTT and were heated at 95℃ for 5 min. For SDS-PAGE, 15–30 μl aliquots of samples were loaded into individual lanes and separated on a precast polyacrylamide gel (10%–18%, Bio-Rad, Hercules, CA, USA) at a constant voltage of 200 V for 30–45 min. Protein bands were then transferred to a 0.2 μm polyvinylidene difluoride (PVDF) membrane (Bio-Rad) by electro-blotting at a constant current of 1.3 A for 5 or 7 min, using a rapid transfer system (Trans-Blot Turbo, Bio-Rad) . After transfer, western blotting was performed with a protein detection system (SNAP i.d. 2.0, Merck Millipore, Billerica, MA, USA). Blots were blocked against nonspecific reactions with 0.5% (w/v) nonfat dried milk or 1% (w/v) bovine serum albumin, diluted in Tris-buffered saline containing either 0.1% (v/v) Tween 20 (TBS-T), or with PVDF Blocking Reagent (Can Get Signal, Toyobo). Blots were then incubated overnight at 4 ℃ with antibodies directed against NGF (sc-548, Santa Cruz Biotechnology, CA, USA), GDNF (sc-328, Santa Cruz Biotechnology), MuRF1 (ab77577, Abcam, Cambridge, MA, USA), Beclin1 (PD017, MBL International Corporation, Nagoya, Japan) or Atg5–Atg12 (PM050, MBL International Corporation). Blots were then washed, incubated with the appropriate secondary antibodies and washed again. Stained bands were then visualized using the ECL Prime Western Blotting Detection System (RPN2232, GE Healthcare Japan, Tokyo, Japan) according to the manufacturer's instructions. Images were captured and documented with a CCD system (Light Capture II, Atto). After measurements, membranes were stripped using stripping buffer (Restore Plus, Pierce, Rockford, IL, USA) and stained with Coomassie Brilliant Blue (CBB) to verify equal loading in all lanes [40]. Densitometric analysis of these images was performed using imaging analysis software (CS analyzer 3.0, Atto) and normalized to the optical density of the CBB stain of each band.

Enzyme-linked immunosorbent assay (ELISA)
Tissue lysates from the Control group at 6 weeks (n = 5) and Task group at 6 weeks (n = 5) were analyzed using an ELISA kit for rat TNF-α (Ray Biotech, Norcross, GA, USA), following the manufacturer's protocol. The minimum assay sensitivity for TNF-α was 25 pg/ml. Data (pg protein) were normalized to μg total protein.

Statistical analysis
Values are presented as means ± standard error of the mean (SEM). Comparison of body weights, grip strengths and mechanical hyperalgesia values were performed by two-way repeated analysis of variance (ANOVA), followed by Holm-Sidak multiple comparison tests. Other comparisons were analyzed using Student's t-test, for time-matched data from two groups. For transparency, both significant differences ($P < 0.05$) and trends ($0.05 \leq P < 0.1$) are reported, where appropriate. A P value of < 0.05 was considered significant. Data were analyzed using SigmaStat 4.0 statistical software (Systat Software Inc., San Jose, CA, USA) .

Results :

Parameters from the voluntary repetitive reaching and grasping task
The rats performed approximately 4,000 reaches and grasps during the first week and approximately 2,000 additional reaches and grasps during each subsequent week (Table 1). As a result, the total number of reaches and grasps throughout the experimental period exceeded 14,000. There were more reaches and grasps during the first week, compared with other weeks, because the rats attempted the task even when pellets were not delivered. Beginning in the second week, rats attempted the reach only when pellets were distributed. In total, the rats obtained approximately 1,100 food pellets per week. Thus, the total number of food pellets obtained reached approximately 6,600 throughout the experimental period. The rats participated in the task for an average of approximately 5.6 h each week, or approximately 34 h throughout the 6-week experiment.

Body weight and grip strength
Body weights gradually increased in both Control and Task groups from week 0 (204.7±2.7 and 215.3±2.4 g, respectively) to week 6 (231.7±6.1 and 237.5±3.0 g, respectively). There were no significant differences in body weight between Control and Task groups. In the Control group, grip strengths did not change, compared with those at week 0, throughout the experimental period (Fig. 3). In the Task group, grip strengths declined significantly from week 2 to week 6, compared with at week 0 ($P < 0.05$) and were significantly lower than in the Control group at 6 weeks ($P < 0.01$). Grip strengths of the Task group decreased rapidly until week 3 and maintained an approximately 25% decrease, compared with initial values, from week 3 to week 5. The maximum decrease in grip strength in the Task group was evident at 6 weeks, a 32.4% decrease.

Forearm flexor withdrawal threshold
Muscle mechanical hyperalgesia was measured as forearm flexor withdrawal threshold values. In the Control group, forearm flexor withdrawal thresholds did not change, compared with those at week 0 (Fig. 4). In the Task group, forearm flexor withdrawal thresholds declined significantly from week 3 to week 6, compared with initial values ($P < 0.05$). These values were significantly lower than those in the Control group from week 2 to week 6 ($P < 0.05$). Forearm flexor withdrawal threshold values for rats in the Task group were gradually decreased up to 6 weeks. The maximum decrease in forearm flexor withdrawal threshold in the Task group was that measured at 6 weeks, a decrease of 11.0%, compared with initial values.

Morphological analysis of FDS muscle
Relative muscle weight (ratio of muscle wet weight normalized to body weight) and muscle fiber CSA values of FDS were not significantly different between the two groups at 3 weeks (Fig. 5 A and B). However, both values were significantly lower in the Task group than in the Control group at 6 weeks ($P < 0.05$ and $P < 0.01$, respectively).

NGF, GDNF and TNF-α expression in FDS muscle
The neurotrophic factors NGF and GDNF and the inflammatory cytokine TNF-α have been implicated in muscle mechanical hyperalgesia [16, 19, 41, 42]. We found no significant differences, between Control and Task groups, in NGF or GDNF mRNA levels at 3 and 6 weeks (Fig. 6 A and B). Consistent with this, western blotting showed no differences in NGF and GDNF protein levels in the two groups at 6 weeks (Fig. 6C). There were also no differences in TNF-α levels, determined by ELISA, in the two groups at 6 weeks (Fig. 7).

Expression of ubiquitin-proteasome and autophagy-lysosome related proteins in FDS muscle
MuRF1 and Atrogin-1 were identified as two muscle-specific E3 ubiquitin ligases, part of the ubiquitin-proteasome pathway, that were increased transcriptionally in skeletal muscle under atrophy-inducing conditions. Beclin1 mediates accumulation of Atg proteins, such as the Atg5–Atg12 conjugation and LC3 conjugation systems, located in pre-autophagosomal structures. Such factors are considered essential for formation of the autophagic vesicle and for triggering autophagy and phagophore formation. At 3 weeks, expression of E3 ubiquitin ligases and Atg genes were not significantly different in the Control and Task groups (Fig. 8A). At 6 weeks, the Task group had significantly higher mRNA levels of MuRF1 and Beclin1, compared with the Control group ($P < 0.05$) (Fig. 8B). The Task group also had higher levels of Atg5 mRNA ($P = 0.071$). Based on these qRT-PCR results, we examined protein levels, at 6 weeks, of only those molecules showing differences in mRNA expression in the two groups.
By western blotting, rats in the Task group had higher levels of MuRF1 protein than those in the Control group at 6 weeks ($P = 0.065$) (Fig. 9). The Task group also had significant overexpression of the Atg proteins Beclin1 and Atg5–Atg12, relative to the Control group, at 6 weeks (both $P < 0.05$).

Discussion :

Change in grip strength across 6 weeks
It was reported that continuing highly repetitive (at least once every 15 s) reaching and grasping tasks for 2 h/day, 3 days/week decreased forearm grip strength in rats, beginning at 6 weeks [5, 43]. These previous studies were not designed to detect an effect at 3 weeks, though Coq *et al.* did include a 1-week timepoint. Therefore, in our experiment, we followed previously described methodology but investigated changes in grip strength in more detail, including at 2 and 3 weeks timepoints. We observed, for the first time, that the decline in grip strength caused by the repetitive tasks occurred earlier than the previous study was able to discern.

Muscle mechanical hyperalgesia caused by repetitive reaching and grasping tasks
We found, also for the first time, that repetitive reaching and grasping tasks caused muscle mechanical hyperalgesia in the rats beginning at 2 weeks. In humans, previous research showed that 23% of female workers in highly repetitive jobs reported muscle pain in the forearm and hand muscles [1]. In rats, it was shown that performance of a high repetition (at least once every 15 s) handle-pulling (force criterion 60± 5% of maximum voluntary force) task resulted in decreased withdrawal threshold values in the forepaws at 6 weeks [44]. Other animal studies showed that skin pain resulted from highly repetitive tasks, with even higher force than those used in our experiment [45]. Our study showed that forearm flexor withdrawal thresholds were significantly decreased from week 3 to week 6, compared with at week 0. These values were significantly lower in the Task than that in the Control group from week 2 to week 6. Based on these results, we determined that a rat model of voluntary repetitive reaching and grasping tasks induced musculoskeletal disorders with forearm muscle pain.

Factors associated with loss of grip strength
Examining the relationship between loss of grip strength and muscle pain, Beyreuther *et al.* reported that intramuscular injection of TNF-α caused muscle pain and decreased grip strength in rats [46]. These investigators also showed that intramuscularly injected lacosamide or gabapentin, both having antihyperalgesic effects, improved grip strength in the presence of intramuscularly injected TNF-α in rats. Thus, muscle pain was a contributing factor in the declined grip strength. In our study, declines in both grip strength and forearm flexor withdrawal in the Task group occurred from week 2 to week 6. These results indicated that one of the potential factors in the decline in grip strength caused by repetitive reaching and grasping tasks was muscle pain. Additional factors, relevant to extracellular matrix proteins and fibrosis, were implicated in repetitive reaching and grasping tasks. Abdelmagid *et al.* [7] reported an increase in collagen type I in skeletal muscle in rats performing the reaching and grasping tasks for 9 weeks. Frara *et al.* [47] observed increased matrix metalloproteinase levels in skeletal muscle of rats performing the tasks for 3 or 6 weeks. Cabrera et al. [48] showed increased collagen type I in skeletal muscle after repetitive reaching and grasping tasks, and attributed muscle fibrosis to the muscle weakness. In our study, the grip strengths of rats in the Task group were lowest at 6 weeks. We observed no morphological changes in FDS muscle at 3 weeks in the Task group rats, compared with the Control group. However, relative muscle weight and muscle fiber CSA of FDS muscle were

significantly decreased in Task group rats at 6 weeks. Previous studies indicated a strong correlation between muscle force and muscle volume or CSA [23–25]. Thus, our findings suggested that the loss of grip strength in the Task group at 6 weeks may have been caused not only by muscle mechanical hyperalgesia, but also by muscle atrophy.

Molecular mechanisms underlying FDS muscle atrophy

The balance between protein synthesis and degradation determines whether a muscle undergoes hypertrophy or atrophy. It was previously demonstrated that chronic low frequency stimulation (10 Hz, 10 h/day) decreased rat extensor digitorum longus (EDL) muscle weight after 4 weeks [49]. Katzeff *et al*. reported, using rats, that long-term (4 weeks) voluntary wheel running decreased protein synthesis rates of the gastrocnemius, but not the soleus, muscle [50]. Cunha *et al*. reported that a single session of running exercise, until exhaustion, in mice activated the 26S proteasome, leading to protein degradation in the plantaris muscle immediately after exercise. This was no longer activated at 48 h after the exercise session [32]. Moreover, these investigators reported that the effects of long-term (8 weeks) running exercise in mice, also activation of the 26S proteasome in plantaris muscle, persisted until even 48 h after the last exercise. Hence, in fast-twitch muscles, long-term repetitive low intensity muscle contraction may cause skeletal muscle atrophy by decreasing protein synthesis and increasing protein degradation. FDS muscle in the rat is known to have a high content of fast-twitch fibers [51]. Overall, the FDS muscle atrophy induced by long-term repetitive reaching and grasping tasks (that is, long-term repetitive muscle contraction) likely resulted from decreased protein synthesis and increased protein degradation.

Two major protein degradation pathways, the ubiquitin-proteasome and autophagy-lysosome systems, are activated during muscle atrophy and contribute, to varying extents, to loss of muscle mass. In the ubiquitin-proteasome system, E3 ubiquitin ligase (MuRF1) can negatively regulate skeletal muscle mass. Long-term (8 weeks) running exercise in mice elicited increased MuRF1 protein expression and 26S proteasome activity in plantaris muscle [32]. Several studies showed that excessive autophagy activation aggravated muscle wasting [52–55]. Long-term (4 weeks) voluntary wheel running in mice led to increased expression of Beclin1 and LC3II proteins in plantaris muscle [33]. Our results showed that long-term (6 weeks) repetitive reaching and grasping tasks increased expression of MuRF1, Beclin1 and Atg5–Atg12 proteins, suggesting induction of the ubiquitin-proteasome and autophagy-lysosome systems in FDS muscle. Moreover, overexpression of MuRF1, Beclin1 and Atg5, at both mRNA and protein levels, coincided temporally with FDS muscle atrophy in the Task group at 6 weeks. Consequently, we propose that activation of the ubiquitin-proteasome and autophagy-lysosome systems contributed to FDS muscle atrophy in the Task group.

Relationship between muscle mechanical hyperalgesia and NGF, GDNF and TNF-α levels in FDS muscle

NGF, GDNF and TNF-α produced muscle mechanical hyperalgesia when injected into skeletal muscle [16, 19, 41, 42]. In addition, upregulation of NGF and GDNF in EDL muscle was essential to mechanical hyperalgesia in an animal model of DOMS, caused by repeated lengthening contractions [15, 16]. DOMS after intense acute swimming, leading to upregulated TNF-α in soleus muscle, was required for mechanical hyperalgesia [11]. Accordingly, we measured NGF, GDNF and TNF-α levels in FDS muscle to investigate the mechanism of muscle mechanical hyperalgesia caused by continuing repetitive reaching and grasping tasks. Barbe *et al*. reported that performance of voluntary repetitive reaching and grasping tasks increased TNF-α levels in rat forearm flexor muscle at 8, but not at 6 weeks [5, 43]. In our study, NGF, GDNF and TNF-α mRNA and protein levels in the Task group were not significantly increased at 3 or 6 weeks, times when muscle mechanical hyperalgesia occurred. The observation that TNF-α protein levels did not change in FDS muscle before 8 weeks was consistent with previous findings [5, 43]. Therefore, we concluded that muscle mechanical hyperalgesia, resulting from continuing repetitive reaching and grasping tasks from week 3 to week 6 may not have been caused by NGF, GDNF or TNF-α . This interpretation is consistent with those of Xin *et al*. [11], who reported that inflammation and pain in a WMSD model (albeit using a different force magnitude from that in our study, that is, a difference in intensity in task performance,) do not involve the same pathway. Elliott *et al*. showed that performance of voluntary repetitive reaching and grasping tasks increased levels of substance P and its preferred receptor, neurokinin-1, in the spinal cord dorsal horn at 6 weeks [10]. Intense noxious stimuli induce substance P release from the central terminals of dorsal root ganglion neurons. Substance P then binds to the neurokinin 1 receptor and sensitizes dorsal horn neurons. Thus, central sensitization may have contributed to the muscle pain in rats performing the voluntary repetitive reaching and grasping tasks. Further study will be necessary, investigating the roles of not only skeletal muscle, but also the central nervous system, in muscle pain caused by repetitive tasks.

In conclusion, our study demonstrated that long-term exposure to excessive repetitive motion caused loss of grip strength, muscle pain and skeletal muscle atrophy. These findings indicated that muscle pain can trigger a loss of grip strength within a relatively short experimental period and that skeletal muscle atrophy and muscle pain are both involved. Furthermore, such exposures may enhance protein degradation through the ubiquitin-proteasome and autophagy-lysosome systems, thereby decreasing skeletal muscle mass.

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Author contribution statement :

Mitsuhiro Fujiwara, Shigeyuki Suzuki, Masahiro Iwata and Takayuki Inoue conceived and designed the project. Mitsuhiro Fujiwara, Masahiro Iwata, Yosuke Aizawa, Natsumi Yoshito and Kazuhiro Hayashi acquired the data. Mitsuhiro Fujiwara, Shigeyuki Suzuki and Masahiro Iwata analyzed and interpreted the data and wrote the paper.

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Table :

Table 1. Parameters from voluntary repetitive reaching and grasping task.

	1 week	2 weeks	3 weeks	4 weeks	5 weeks	6 weeks
Total reaches and grasps (n)	4019.0 ± 533.5	6682.2 ± 775.5	8909.0 ± 974.9	10904.2 ±1161.1	12853.5 ± 1313.7	14758.3 ± 1459.7
Total food pellets obtained (n)	1047.7 ± 60.3	2117.8 ± 88.1	3267.0 ± 116.8	4355.0 ± 176.1	5457.5 ± 235.4	6579.2 ± 292.8
Total task duration (h)	5.6 ± 0.3	11.2 ± 0.5	17.0 ± 0.7	22.6 ± 1.0	28.2 ± 1.2	33.9 ± 1.3

Data are presented as mean ± standard error of the mean.

Figure legends :

Fig. 1. Voluntary repetitive reaching and grasping for food pellets. During the task, the rat repeatedly performs the action shown in the photograph once every 15 s (A-D) . (A) The food pellet is dispensed on the shelf attached to the test box placing the rat. (B and C) The rat reaches and grasps for the food pellet placed on the shelf. (D) The rat eats the food pellet grasped in its paw.

Fig. 2. Mechanical hyperalgesia analysis measuring forearm withdrawal threshold. Two photographs illustrate the procedure, as described in detail in the Materials and Methods. Each rat, with head and trunk covered, was suspended in a homemade hammock (left). This position allowed the forelimbs to freely move, with the arrow indicating the direction of mechanical forces applied to the forearm flexors (right).

Fig. 3. Changes in grip strength. Data are means± standard error of the mean. $^{*}P < 0.05$, $^{**}P < 0.01$, compared with week 0. $^{a}P < 0.05$, $^{aa}P < 0.01$, compared with time-matched rats from the Control group, (n = 6 per group).

Fig. 4. Change in forearm flexor withdrawal thresholds. Data are means ± standard error of the mean. $^{*}P < 0.05$, $^{**}P < 0.01$, compared with week 0. $^{a}P < 0.05$, $^{aa}P < 0.01$ compared with time-matched rats from Control group, (n = 7 in Control group and n = 10 in Task group).

Fig. 5. Morphological changes in flexor digitorum superficialis (FDS) muscles at 3 and 6 weeks. (A) Relative muscle weight; (B) Muscle fiber cross-sectional area (CSA). Data are means± standard error of the mean. $^{*}P < 0.05$, $^{**}P < 0.01$, compared with time-matched rats from Control group, (n = 6 per group).

Fig. 6. Expression of neurotrophic factors in flexor digitorum superficialis (FDS) muscles. (A) nerve growth factor (NGF) and glial cell line-derived neurotrophic factor (GDNF) mRNA expression at 3 weeks (n = 6 per group); (B) NGF and GDNF mRNA expression at 6 weeks (n = 5 per group); (C) NGF and GDNF protein expression at 6 weeks. Representative blots depicting NGF and GDNF are shown. Quantitative analysis is shown in the lower panel. Results are reported as fold changes with respect to control levels, which were arbitrarily set to 1. Data are means ± standard error of the mean. CBB, Coomassie brilliant blue staining for total protein.

Fig. 7. Expression of tumor necrosis factor (TNF) -α protein in flexor digitorum superficialis (FDS) muscles at 6 weeks. Data are means ± standard error of the mean, (n = 5 per group).

Fig. 8. mRNA expression of E3 ubiquitin ligases and autophagy-related (Atg) genes in flexor digitorum superficialis (FDS) muscles. (A) At 3 weeks. (B) At 6 weeks. Results are reported as fold changes with respect to control levels, which were arbitrarily set to 1. Data are means ± standard error of the mean. $^{*}P < 0.05$, compared with time-matched rats in Control group, (n = 6 per group). MuRF1, Muscle RING finger 1; Atrogin-1, Muscle atrophy F-box/Atrogin-1; Atg, Autophagy-related; LC3, Microtubule-associated protein 1 light chain 3.

Fig. 9. Levels of muscle RING finger 1 (MuRF1), Beclin1 and autophagy-related (Atg) 5-Atg12 proteins in flexor digitorum superficialis (FDS) muscles at 6 weeks. Representative blots depicting MuRF1, Beclin1 and Atg5-Atg12 are shown. Quantitative analysis is shown in the lower panel. Results are reported as fold changes with respect to control levels, which were arbitrarily set to 1. Data are means ± standard error of the mean. $^{*}P < 0.05$, compared with time-matched rats in Control group, (n = 6 per group). CBB, Coomassie brilliant blue staining for total protein.

ワークショップ
当院におけるカプセル内視鏡読影の実際
～カプセル内視鏡読影精度の向上を目指して～

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【背景と目的】
当院は名古屋大学消化器内科の指導の下、2010年4月よりカプセル内視鏡（以下 CE）読影センターを開設した。読影センターには常に速さと正確性が要求されると考えている。本センターの特徴は、オンライン画像転送及び、読影支援技師の一次読影と内視鏡医の二次読影である。以前当学術集会において、読影終了までの時間について検討し、特に出血例で迅速に対応していることを報告した。今回は、読影センターに要求されるもうひとつの重要な因子である読影の正確性について、そのための読影精度の向上に観点をおき検討した。
読影センターにとって、その読影の正否を知ることは非常に重要である。そこで、提携病院に読影後の経過についてのアンケート調査を行い、その結果をもとに検討したことを報告する。
【対象と方法】
2012年3月から2014年10月に読影した279症例中要精査の88症例を対象とし、精査の有無・方法・結果等についてアンケート調査を実施した。
【結果】
78症例の回答があった。精査せず36症例、記入なし2症例で、精査後の結果が判明したものが40症例であった。そのうち、①精査にて確定診断した病変を CE読影で指摘できた症例が27症例、② CE読影で病変を疑ったが精査で異常がなかった症例は13症例、③精査にて確定診断した病変を CE読影では指摘できなかった症例は無かった。しかし①の中には、CE読影で存在の指摘はできていたが、精査結果は異なる病変という症例も含まれる。読影にて Angioectasia及び腫瘍か動静脈奇形を疑ったが Angioectasia のみであった症例や、読影にてクローン病を疑ったが精査では小腸 MALT リンパ腫であった症例などである。（後者は、胃内の不整びらんの指摘から胃癌も診断された。）
【考察】
今回の検討では、当院読影センターの読影にて過剰に指摘していることもあるが、少なくとも病変の存在は指摘できていると考えられた。CE の特性上確定診断に至ることはむずかしいことも多く、その点では CE検査や読影の目的は達しているように判断できた。今回は読影センターで指摘した症例のみの検討であり、読影センターで精査不要と判断した症例が含まれておらず、今後はすべての症例を網羅して調査する必要はある。
【結語】
読影センターにとって、読影精度向上のためには、精査結果の情報共有が重要と思われた。

発表　第10回日本カプセル内視鏡学会学術集会　ワークショップ
名古屋市 2017年2月18日

大腸内視鏡検査の前処置にラジオ体操がもたらす効果の検証

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【目的】
大腸内視鏡検査の前処置は、前処置が完了するまでの身体的・精神的苦痛を伴う。A病院では、2時間以内に前処置が完了しない場合は追加処置を行っており、患者は更なる苦痛を強いられている。患者の負担を少しでも軽減するため、大腸の蠕動運動と排便促進の関連性に着目し、誰もが親しみのあるラジオ体操が、前処置にどのような効果をもたらすかを検証する。
【方法】
2013年5月20日～ 2015年8月1日にかけて、A病院で大腸内視鏡検査を受け、前処置にモビプレップを使用し、追加処置のなかった265名を対象とした。前処置完了までに要した時間を、ラジオ体操導入前後で比較した。また、ラジオ体操導入後の患者には、ラジオ体操に対するアンケートを実施し、感想を得た。
【成績】
総数は265名で、ラジオ体操導入前57名、導入後208名であった。導入前の前処置完了までの平均時間は136.05分、導入後は130.11分であった。患者アンケートでは、楽しかった29.8%、気分転換になった72.5%、気持ちよかった27.8%、辛かった0.03%、面倒だった0.004%と回答した人より多くなった。また、便が出たと感じた人は47.5%であった。
【結論】
患者の前処置への身体的負担や精神的苦痛を軽減したいと考え、誰もが親しみのあるラジオ体操を取り入れ、効果を検証した。ラジオ体操により、大腸の蠕動運動促進に効果が得られ、前処置完了時間が5.94分減少することができた。また、患者の実感として、便が出たと感じる人や気分転換になると感じる人が多く、精神的な援助に繋がることが示唆された。そのため、今後もラジオ体操を継続して行い、前処置完了時間の短縮や精神的苦痛への援助の一つとして、継続して行っていく。

発表　第67回日本病院学会　一般演題　神戸市　2017年7月21日

予定大腸癌手術の手術部位感染症対策による術後合併症減少効果についての検討

The evaluation of our perioperative managements to reduce SSI in elective colorectal surgery.

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#1：総合上飯田第一病院

【目的】
当院は地域に根差した2次病院であり、大腸癌手術症例は、高齢者・イレウス発症や内視鏡不通過例・非治癒切除例が多く、多数の併存症や術前低栄養状態の患者も含まれている。以前より手術部位感染症（SSI）の頻度が高かったため、2016年より周術期対策を強化し、その効果を検討した。
【方法】
2012年1月から2015年12月の症例検討（第116回、日本外科学会定期総会にて発表）を踏まえ、2016年1月より、①術前対策：低栄養患者（Alb 3.5g/dl未満）に対する積極的栄養治療、手術前日のシャワー浴。②術中対策：Wound protector（WP）使用、手袋交換、術中抗生剤追加投与、直腸癌症例に経肛門チューブ留置、閉創時の器械交換などを行った。2012年1月から2016年10月の間に行った予定大腸癌切除手術237例を2015年まで195例（A群）と2016年の42例（B群）にわけて検討。
【成績】
全症例の年齢中央値は72歳（30-93歳）、男性141例女性96例。疾患は結腸癌150例（63%）、直腸癌87例（37%）。内視鏡不通過は103例（44%）、イレウス発症は49例（21%）であった。術後合併症は、Clavian-Dindo（CD）2以上105例（44%）、CD3a以上46例（19%）、感染性合併症83例（35%）、全 SSI　72例（30%）、手術切開部位 SSI（I-SSI）49例（19%）、Stoma閉鎖創を除く創の I-SSI 46例（19%）、Stoma閉鎖創3例 /18例（16%）、体腔臓器 SSI42例（17%）、縫合不全35例（15%）、遠隔感染症22例（10%）、イレウス29例（12%）、譫妄30例（12%）、再手術16例（7%）、術後在院死亡4例（1.7%）であった。
術前因子、年齢・性別・部位・ASA・PS・術前アルブミン値、小野寺 PNI・内視鏡不通過・イレウス発症・原発部位は群間に有意差を認めなかった。術後合併症率（A群 /B群、p値）は、CD2以上（44%/47%,p=0.63）、CD3a以上（18%/23%, p=0.42）、感染性合併症（36%/31%, p=0.54）、全 SSI（32%/24%, p=0.30）、I-SSI（21%/19%,p=0.77）、Stoma閉　鎖創を除く創の I-SSI（20%/14%, p=0.35）、stoma閉鎖創（8%/20%, p=0.34）、体腔臓器 SSI（19%/9%, p=0.12）、縫合不全（17%/7%, p=0.12）、遠隔感染症（9%/9% p=0.95）、イレウス（12%/11%,p=0.94）、譫妄（10%/24%, p=0.017）、再手術（7%/5%, p=0.57）、術後在院死亡（1%/2.4%, p=0.47）。有意に減少した項目は認めなかったが、Stoma創を除く創の I-SSI と縫合不全は減少傾向にあった。
【結論】
今行っている対策では不十分と考えられた。危険因子を再度検討し、また対策一つ一つの遵守率の検討などを行い、より術後合併症減少へのプランを立てる必要がある。

第72回　日本消化器外科学会総会　金沢　2017年7月21日

緩和ケアチームによるがん療養支援イメージ
～男も女もその人らしく、ともに生き切るために

岡島明子

総合上飯田第一病院　外科・緩和ケアセンター

　演者は中規模急性期総合病院に外科医として赴任し、5年前から緩和ケアチームリーダーとして一般病床における緩和ケアを積極的に行ってきた。入院介入は年間約200例、看取りは月に平均約10件程度まで増加した。その中で見えてきた支援イメージについて、性差との関連を述べてみたい。
緩和ケア介入の目的は単に症状の緩和にとどまらず、患者さんがその人ら

しさを保ち、残された日々を家族とともに納得のうちに生き切ることだと考える。そのためには、終末期ではなく診断時や抗癌治療中から関わっていくことが望ましい。その内容は、患者さんの性差と家族構成によって焦点を変えて行うのがよいと思われる。
例えば、女性患者はたとえ独居であっても身内、友人らと何等かの関わりを続けていることが多く、完全に孤立した生活にはなりにくい。かなり病状が進行するまで自分自身で衣食住を管理し、現実の生活を保っていく力を感じる。本人が病状を受容したうえで、「治療は希望せず、痛みだけをとってほしい」「迷惑をかけたくない、ホスピスに入る」など自分から尊厳を持って宣言されることも多い。よって女性患者に対しては、精査・抗癌治療・終末期の様々なステージにおいて、その方らしさを安心して全うできるように選択を支援していくことが重要と思われる。
一方、男性患者は抗癌治療の終了を医師が勧告してもなお闘い続けることを望む傾向がある。多くが、積極的治療中止や緩和ケアの推奨、介護サービスの提案に対して怒りの反応を見せる。しかし、毎日の食事など生活の基本的な所には比較的無頓着で、消耗しきって緊急入院になり、ようやく抗癌剤中止や介護支援を受け入れるケースが目立つ。特に食欲の落ちる抗癌剤治療中や、疼痛増悪の時期には、栄養面や心理面で注意深い支援を要する。苛立ちや怒りを家族やスタッフにぶつけることもよくあり、これは本来病気に向けられるべき感情であると理解して向き合うことが重要である。
また家族側に配慮すべき性差として、女性が妻・嫁・娘等の立場にある場合、家事・育児・介護は当然女性の仕事と思われているため無意識に重い負担がかかっている。逆に介護者に夫・兄弟・息子などの男性しかいない場合、衣食住や服薬の管理はかなり手薄になる可能性が高い。仕事の責任もあるため医療チームや本人との絆も、淡々としたものになりがちである。それを考慮した上でケアプランを考える必要がある。

第10回日本性差医学・医療学会学術集会　名古屋　2017年1月28日

腋窩リンパ節転移で見た化学療法の有効性の検討

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総合上飯田第一病院 乳腺外科

腋窩リンパ節転移陽性個数の増加に伴い予後が悪くなることが知られており、腋窩リンパ節転移数は重要な予後予測因子とされている。しかし、当院で検討した腋窩リンパ節転移陽性1個から3個（n1α）の予後は腋窩リンパ節転移陰性（n0）乳癌と有意差がなく、n0乳癌とn1α乳癌を比較することで、乳癌治療の意義を再考した。
【方法】
2006年1月より2012年12月に手術を行った原発性乳癌618例中、両側乳癌、非浸潤癌、浸潤径5mm以下の微小浸潤癌、詳細不明例を除いた391例を検討した。観察期間は107 ～ 3975日（中央値2187日）で、生存率は補正生存率とした。subtypeにおいて2009年6月以前の症例はKi-67の測定を行っておらずluminal AとBは合わせて検討した。
【結果】
n0：278例、n1α：78例、n1β：35例あり、それぞれの5年 ,8年生存率はn0群98.7%,97.2%、n1α群97.2%,95.0%、n1β群63.6%,55.0% で、n0群とn1α群に有意差は見られなかった。化学療法を施行した症例はn0群61例、n1α群56例、n1β群31例あり、生存率で比較すると、化療なしではn0群で有意に成績が良かったが、化療ありでは有意差はなかった。n1β群は化療あり、なし関係なく予後が悪かった。subtypeによる検討では、luminal type（L群）は266例、luminal HER2 type（LH群）は11例、HE2 type（H群）は31例、Triple Negative type（TN群）は83例あり、生存率はそれぞれの群で有意差はなく、化療の有無での比較でも生存率に差はなかった。当院では標準治療として、n0 high risk、n陽性症例では、アンスラサイクリン系もしくはタキサン系主体の補助化学療法を行っているが、色々な要因で標準治療が行えなかった症例を過少療法群（89例）として比較検討すると、n0群では生存率に差がなかったが、n1α群では標準と過少療法群で有意差 p=0.056と過少療法群で治療成績が悪い傾向にあり、n1β群では有意に過少療法群で成績が劣った。無再発生存率では、n0群、n1α群、n1β群の順に有意に低下していたが、それぞれの群において化療の有無による差は見られなかった。また、化療の程度（標準群、過少群）による差も見られなかった。
【まとめ】
乳癌においてn因子は重要な予後予測因子であるが、n0乳癌とn1α乳癌での生存率で差がなく、無再発生存率では差が見られたことは、近年の再発後治療の進歩でn1α乳癌の予後が改善されている結果と思われた。特に、リンパ節転移陽性群において標準化学療法の重要性が示唆された。

第25回日本乳癌学会　福岡　H29年7月13日～ 7月15日

マンモグラフィでの乳腺濃度から見た乳癌の検討

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マンモグラフィ診断において高濃度乳房は診断感度が低いことが知られている。当院での乳癌手術例において、乳房構成別の乳癌の特徴を検討した。
対象は、2010年から2016年に当院で手術を行った原発性乳癌症例の中でマンモグラフィを検討し得た651例。乳房構成は、脂肪性26例、散在性229例、不均一高濃度353例、極めて高濃度43例であった。年齢は脂肪性が45 ～ 90歳（平均74.3歳）、散在性は35 ～ 98歳（平均66.4歳）、不均一高濃度は30 ～ 86歳（平均53.0歳）、極めて高濃度は26 ～ 76歳（平均44.9歳）であった。BMI平均値は脂肪性25.7、散在性23.4、不均一高濃度21.4、極めて高濃度20.0であった。検診発見（他自覚症状で偶然発見例を含む）症例は、脂肪性7例（26.9%）、散在性92例（40.2%）、不均一高濃度209例（59.2%）、極めて高濃度25例（58.1%）であった。マンモグラフィ主所見は、極めて高濃度で16例（37.2%）は所見なしで、13例は石灰化であった。不均一高濃度でも51例（14.4%）は所見なしであった。脂肪性では所見なしは0例、散在性では18例（7.9%）と高濃度乳房よりは所見なし症例は有意に少なかった。組織結果での非浸潤性乳管癌の割合は、脂肪性15.4%、散在性15.3%、不均一高濃度26.3%、極めて高濃度30.2% であった。
高濃度乳房で見つかる乳癌は自覚症状で見つかることが多く、非浸潤性乳管癌の割合が高かった。

第79回　日本臨床外科学会抄録
登録番号：11866（H29年11月23日-11月25日　東京）

高濃度乳房の診断

窪田智行

総合上飯田第一病院　乳腺外科

最近話題の高濃度乳房の診断について症例を提示し検討する。
マンモグラフィ診断において高濃度乳房は診断感度が低いことが知られており、米国では近年、マンモグラフィ検診受診者に対して乳房構成を通知する動きも出てきている。そのような情勢の中、平成29年3月21日付で日本乳癌学会、日本乳癌検診学会、日本乳がん検診精度管理中央機構の連名で、対策型乳がん検診における「高濃度乳房」問題の対応に関する提言が出された。提言の内容自体は、乳房構成の受診者への通知は時期尚早であり、対策型検診における乳房超音波検査の併用はまだ検討段階であるというものであるが、このような高濃度乳房の診断において、何に注意し診断をしたら良いのかを、症例を通して考えて行きたい。
乳癌の画像診断において、マンモグラフィ、乳房超音波検査はともに必須の検査手段であるが、高濃度乳房の場合、マンモグラフィにおける病変の検出感度は低下する。当院2010年から2016年の原発性乳癌症例において、43例の乳腺濃度が「極めて高濃度」の乳癌症例のマンモグラフィ主所見は、16例（37.2%）は所見なしで、13例は石灰化であった。「不均一高濃度」353例中でも51例（14.4%）は所見なしであった。もちろん病変の検出感度は乳癌腫瘤径の大きさに左右される面もあるが、しかし「脂肪性」26例では所見なしは0例、「散在性」229例中では18例（7.9%）と高濃度乳房よりは所見なし症例は有意に少なかった。
症例を振り返りながら、高濃度乳房の実態を把握し、診断に対してどのような点を注意するのか、見落としとならないためのコツを探って行きたい。

第14回　日本乳癌学会中部地方会（教育セミナー）
長野県飯田市　H29年9月9日

脊髄硬膜外動静脈瘻の血管解剖と治療 —脊髄硬膜動静脈瘻との比較—

Angioarchitecture and treatment of spinal epidural arteriovenous fistula – comparison with spinal dural fistula-

Key words：脊髄硬膜外動静脈瘻、脊髄硬膜動静脈瘻、手術、塞栓術、血管解剖
Spinal epidural arteriovenous fistula, spinal dural arteriovenous fistula, surgery, embolization, angioarchitecture

名倉崇弘[1]、宮地茂[2]、松尾直樹[2]、川口礼雄[2]、高安正和[2]

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【目的】
脊髄硬膜外動静脈瘻（SEDAVF）は硬膜外にシャントを有し、脊髄静脈に逆流して静脈鬱滞に伴う myelopathy を呈する疾患である。脊髄硬膜動静脈瘻（SDAVF）と症候は類似しているが、特徴について両者を比較するとともに、治療における問題点について検討した。
【対象と方法】
過去10年間に経験した SEDAVF9例（49-84歳、男性6例）、全例高度の脊髄症状（下肢運動感覚障害、膀胱直腸障害）を呈した。シャント部位は L1-仙椎部で、全例脊柱管腹側に存在し、8例で硬膜外に pouch を伴った。シャント血流は perimedullary vein を上行し、conus level で脊髄静脈に逆流した。治療は3例で経動脈的塞栓術、6例で観血的に drainer の遮断が行われ、全例でシャントの消失を得た。同時期に治療を行った13例の SDAVF例と血管解剖および治療戦略について比較検討した。
【結果】
SEDAVF は SDAVF に比べ尾側（馬尾部）に位置し、シャントは腹側の硬膜外静脈叢の isolated pouch に流入しており、背側の根静脈より直接脊髄静脈に連絡する SDAVF の構造と異なった。さらに術中所見では、硬膜貫通部位は通常腹側根部であるが、そのレベルが pouch より上位であったり、離れた部位にある例もあった。
【考察と結論】
SEDAVF は SDAVF と病態は類似しているが、硬膜外を経由してから硬膜内に流入するユニークな形態をもつ。治療のゴールは drainer である perimedullary vein を閉塞することで達成されるが、塞栓術においては、pouch を通過して drainer まで塞栓物質を到達させる必要があること、観血的治療にでは、硬膜内への drainer の入口部を術前血管撮影にて十分把握しておく必要がある。また通常の血管撮影では描出が困難で、確定診断に長期間有し重篤化する例が多いため、この病態の存在を十分認識しておく必要がある。

第33回日本脳神経血管内治療学会総会　東京　2017年11月23日 -25日

前立腺肥大症の治療薬変更についての検討

総合上飯田第一病院　泌尿器科　服部愼一

前立腺肥大症の治療ではα1-blocker、抗アンドロゲン剤などが利用されるようになり、外科的手術の症例は以前に比べて減少している。併用療法も珍しくないが、患者の希望などで減量や中止を検討しなくてはならないこともある。また最近の例ではメーカーの出荷停止で変更を余儀なくされることもある。今回減量や変更等でどのような変化があるか検証した。
【対象】
排尿障害が強い前立腺肥大症患者でα1-blocker（シロドシン）と5α還元酵素阻害薬（デュタステリド）の内服併用治療を開始した12例を対象。
【方法】
内服前に前立腺サイズ、IPSS と QOL を評価し、内服薬の内容変更時などに再評価し比較する。
【結果】
内服後は前立腺サイズの減少がみられ、排尿スコアを中心に改善が見られた。改善例を中心に5α還元酵素阻害薬の中止を試みるが症状の憎悪は見られず、前立腺サイズの増大傾向もなかった。観察中性欲減退など大きな副作用は見られなかった。
【結論】
α1-blocker と5α還元酵素阻害薬の併用治療後、5α還元酵素阻害薬を中止しても症状の憎悪が見られない可能性がある。

第105回日本泌尿器科学会総会　鹿児島　2017年4月23日

当院での排尿ケアチーム介入による排尿自立の成果について

総合上飯田第一病院　泌尿器科　服部愼一
認定看護師　林佳美
理学療法士　帆澤子　右高沙妃

平成28年度から「排尿自立指導料」が算定可能になり当院でも平成28年7月から排尿ケアチームを作成し排尿自立に向け介入を開始。
【対象及び方法】
平成28年7月～現在の介入患者の原疾患、合併症、介入要請の病態、治療法と転機等を解析し自立の成否ついて検討。
【結果】
病態では尿閉等の排出障害と頻尿等の蓄尿障害がほぼ同等。整形外科患者では体動困難から機能性尿失禁が目立った。当初カテーテル留置や導尿していた患者の約半数は排尿自立が可能になった。
【考察】
排尿ケアチームの介入により職員の意識も変革し排尿が自立可能な患者数が増加すると考える。また排尿の自立で退院先の選択等で有利となり、健康寿命延長等の効果が期待出来る。

第67回日本泌尿器科学会中部総会　大阪　2017年11月25日

名古屋市における水痘ワクチン助成と定期接種普及後の水痘発生動向

先行した助成接種後水痘の季節的な流行は消失プラトーに達した。定期2回接種普及の効果が期待される。

研究代表者または研究分担者
後藤泰浩（総合上飯田第一病院　小児科部長）

研究要旨
名古屋市は2010年8月1歳児から就学前まで約半額の水痘ワクチン単回費用助成制度を開始し、1歳児から3歳前までが10月定期接種となった2014年度まで継続した。この期間の接種勧奨により助成・定期接種は順調に拡大し、2014年度その累積接種率は一歳から就学前人口の76.1% となった。市感染症発生動向調査による水痘報告数は、開始年度以降減少し、2014年度46%、2015・2016年度は37% に止まっている。週別発生数では春先のピークが消失、2015・2016年度は季節性のない小流行の散発になっている。定期接種化に先行する自治体の単回就学前児助成接種制度は、速やかな疾病抑制に貢献しその効果はプラトーとなった。今後は2回接種拡大の効果が期待される。
A. 研究目的
名古屋市の就学前単回費用助成制度・定期2回接種普及が水痘流行に与えたインパクトを評価した。
B. 研究方法
市健康福祉年報に記載された各年の助成・定期接種数の年齢別集計、最近10年間における市内16区の70医療機関から報告された感染症発生動向調査を比較した。
C. 研究成果
一歳から就学前の人口に対する接種率は年々上昇し、費用助成制度を開始当初の11.6% から累積し、個別通知を開始した2013年度54.2%、無料化と定期接種が始まった2014年度76.1% に達した。2015年の定期接種率は一回目が100.5% 2回目が94.9% と高い接種率を示している。水痘報告数は2010年度2,266件から2014年度1,036件、2015年度838件に減少。2016年12月までに前年同数とプラトーに達した。週別の推移を見ると、春先の流行ピークが消失、2015年度以降冬期の目立った流行の波は認められず、季節によらない散発小流行に終始している。
D. 考察
自治体による予防接種費用助成制度と個別通知は高い接種率につながる。水痘においては一歳から就学前児童の累積接種実績50% を超えた時点で減少が著明になり、75% を超え季節・新年度の流行もみられなくなる。今年度には就学前の1回接種がほぼ終了し、定期2回接種者も50% に届くと予想され、今後水痘ウイルス感染の疫学が変貌することが予想される。
E. 結論
定期接種化に先行する自治体の就学前単回助成接種制度は、速やかな疾病抑制に貢献しその効果はプラトーとなった。今後は定期2回接種拡大の効果が期待されると考えられた。
F. 研究発表
1. 学会発表
第19回日本ワクチン学会学術集会
「名古屋市における費用助成による水痘ワクチン普及と流行消失」
H. 知的財産権の出願登録状況
なし

「中枢神経障害性異常感覚」の提案　～疼痛と掻痒～

Central neuropathic dysesthesia：proposal of an entity

鵜飼克行[1、2]

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[2] 名古屋大学大学院医学系研究科精神医学分野

【目的】
パーキンソン病には、しばしば疼痛が伴う。その原因の一つとして、中枢の脳神経細胞の変性に起因するものが推定されている。つまり、脊髄損傷後疼痛や脳梗塞後疼痛と同様に、中枢神経障害性疼痛の一つとみなされている。演者らは平成27年の日本認知症学会において、レビー小体型認知症に伴う中枢の脳神経系変性に起因すると思われる疼痛に対し、少量のプレガバリンが有効であった報告を行った 1)。また、昨年の日本精神神経学会において、レビー小体型認知症に伴う皮膚掻痒症に対しても少量のプレガバリンが著効した症例を報告した 2)。これまでレビー小体病に伴う掻痒に

対しては、ほとんど注意が払われておらず、「中枢脳神経系の変性に起因する掻痒」という概念は、認知症や高齢者医療の分野のみならず、緩和医療や皮膚科領域でも、一般的にはなっていない。
【方法】
中枢脳神経系の変性に起因する異常感覚と思われる上記の4自験例の概要をまとめて提示し、その異常感覚の特徴や発生機序、プレガバリンの作用機序など、できるだけ包括的に文献的な考察を試みる。
【結果】【考察】
本学術総会において、中枢脳神経系の変性に起因する異常感覚、すなわち「中枢神経障害性異常感覚」という仮説的概念を提案するとともに、その文献的考察の結果を供覧したい。

1) Ukai K, Fujishiro H, Ozaki N. Effectiveness of low-dose pregabalin in three patients with Lewy body disease and central neuropathic pain. Psychogeriatrics 2016; doi : 10.1111/psyg.12192.
2) Ukai K. Possible effectiveness of low-dose pregabalin in a patient suffering from Lewy body disease and chronic pruritus. Psychogeriatrics 2016; doi : 10.1111/psyg.12236.

第113回　日本精神神経学会　名古屋　平成29年6月22日

脳波・てんかん関連ワークショップ「認知症の鑑別診断として知っておきたいてんかん」

鵜飼克行[1, 2]

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【目的】
高齢化と共に発症率が急上昇する疾患といえば、直ぐに認知症が思い出されるが、てんかんも同様であることは十分に知られているとは言い難い。この原因として、高齢期に発症するてんかんは、小児てんかんとは特徴が大きく異なっていることも一因であると思われる。本講演において、高齢発症てんかんの特徴、認知症性疾患との類似性と鑑別診断、さらには神経変性性認知症とてんかん性疾患の関係性について、できるだけ包括的にまとめてみたい。
【方法】
文献的な考察を行うとともに、自験症例を提示しての考察も行う。
【結果】【考察】
主に以下の項目につき、検討・考察したい。
(1) 高齢発症てんかんの特徴
(2) 認知症外来における認知症類似てんかん性疾患
　① 非けいれん性てんかん重積（NCSE）
　② 一過性てんかん性健忘（TEA）：“広義の TEA”概念の有用性（1,2）
　③ アルツハイマー病類似の“てんかん性認知記憶障害”（3,4）
　④ 自律神経発作：レビー小体病の呼吸困難感（Sensory dyspnea）とパニック発作
(3) “Subclinical seizures”による症状だけのてんかん性疾患：てんかんの定義上 OK か？
(4) 広義の TEA症候群：レビー小体病の前駆症状か？

1. Ukai K, et al. Similarity of symptoms between transient epileptic amnesia and Lewy body disease. Psychogeriatrics 2017; 17 : 120-125.
2. Ukai K, Watanabe M. Transient epileptic amnesia without epileptic seizures : Proposal of a new entity. Psychogeriatrics 2016; DOI : 10.1111/psyg.12249.
3. Ito M, et al. A case series of epilepsy-derived memory impairment resembling Alzheimer disease. Alzheimer Dis Assoc Disord 2009; 23 : 406-409.
4. 柴﨑一昌。物忘れ外来における高齢初発てんかんの症状と脳波所見。Dementia Japan 2017; 31 : 31-38.

第30回　日本総合病院精神医学会　富山　平成29年11月18日

Possible prodromal symptoms of dementia with Lewy bodies : accelerated long-term forgetting and autobiographical amnesia associated with transient epileptic amnesia

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[3] 新宿神経クリニック

一過性てんかん性健忘（transient epileptic amnesia・TEA）は、中高齢者における側頭葉てんかんの特殊型であり、そのほとんどのケースで accelerated long-term forgetting（ALF）や autobiographical amnesia と呼ばれる極めて特徴的な二つの記憶障害を合併する、比較的稀なてんかん性疾患である。一方、レビー小体型認知症（DLB）は、アルツハイマー病に次いで二番目に多い神経変性性認知症性疾患であり、近年はその前駆期における超早期診断の重要性が認識されつつある。我々は、ALF・autobiographical amnesia を認めた（広義の）TEA の2自験例を経験した（1）。しかも、その2症例は、ともに DLB の前駆期であろうと診断された。すでに我々は、第111回日本精神神経学会（平成27年）において、TEA と DLB の臨床症状の類似性を考察し、両疾患には関連性がある可能性について言及した（2）。今回の発表では、この2自験症例を提示するとともに、超早期段階での Lewy病理が ALF や autobiographical amnesia の発生を引き起こす可能性、すなわち、ALF や autobiographical amnesia が DLB の前駆症状である可能性について指摘する。

(1) Ukai K, Watanabe M. Transient epileptic amnesia without epileptic seizures : Proposal of a new entity. Psychogeriatrics 2016; doi : 10.1111/psyg.12249.
(2) Ukai K, Fujishiro H, Watanabe M, Kosaka K, Ozaki N. Similarity of symptoms between transient epileptic amnesia and Lewy body disease. Psychogeriatrics 2017; 17 : 120-125.

第36回　日本認知症学会　金沢　平成29年11月24日

「院内認定臨地実習指導者研修の実際と課題」

安藤明子

社会医療法人愛生会　総合上飯田第一病院　看護部

A病院は、地域包括ケア病棟40床を含めて236床の中規模病院で看護専門学校を有している。毎年、約30名の卒業生が新人看護師として入職している。また全病棟で常に看護学生の実習を受け入れている。県主催の臨地実習指導者研修を毎年1 ～ 2名受講しているが、新人教育やリーダー業務などもあり臨地実習指導者研修修了者以外の看護師が実習に携わることがある。実際に実習生に関わっている看護師から指導方法や関わり方についての悩みや負担感を聞くことが多い。臨地実習指導者研修受講者の報告会を毎年行っているが、実際に臨地実習指導を行っている看護師の悩みを解消することはできていない現状である。そこで院内で臨地実習研修プログラムを看護部の教育担当師長とともに考え実施した。
臨地実習指導者に必要な要素を「知識・技術・アセスメント力」「共に学ぶ姿勢」「向上心」と考え、そこから“看護する喜び”を自身で再確認し、看護学生に実践してみせることのできる看護師であり、共に看護を考えることの楽しさを研修で実感してもらうことをねらいとした。
A病院は、院内のクリニカルラダーに基づき人材育成を行っている。専門看護師や認定看護師も多くなり、専門領域のスペシャリストして活躍している。また各施設内の「認定制度」を設けている施設も多くなってきている。しかし、その位置づけや認定要件は様々である。今回の研修を実施して、プログラム内で行ったワールドカフェが有効であり、参加した看護師一人一人が成人学習者として自己と見つめることで、成長できたと感じることができた結果であった。しかし、今後の継続教育や認定制度の確立は今後の課題である。

第19回日本医療マネジメント学会学術総会　仙台　2017年7月7日

ROO製剤で疼痛コントロール中、せん妄への対応に難渋した一例

佐藤真嗣

1）総合上飯田第一病院　緩和ケアチーム看護師

40歳代、男性、盲腸癌。1年前に他院にて診断。右半結腸切除術を施行。今回、緩和治療目的で当院へ紹介、転院となった。蝶形骨転移から左目失明、脊椎転移のためコルセット着用し車椅子使用とされていた。
患者は、30歳頃に借金により夜逃げ、その後住居や職を転々としながら、結婚し子をもうけたが、浮気で離婚。しかし発症を機に、元妻が親子の間に入ろうと協力的にサポートをしていた。当院は元妻宅から近く、子供達も面会に来やすいといった理由で希望された。
転院後はオピオイドによる疼痛コントロールを図り、家族の時間を作りながら、自宅に一度は帰るという目標でリハビリに取り組んでいたが、せん妄を発症。オピオイドによる原因だけでなく、もともとの反社会的パー

ソナリティも要因として大きかったと思われる。経過中に、離院、暴言、暴力などの様々な問題行動が出現したが、関わるスタッフで情報交換を密に行い日々対応を行なった。それから亡くなる直前まで、患者家族の目標を支え続けることができた。また、転院や強制退院という方法を取らずに、当院で看取りまでできたことで、当初からの希望であった「家族との時間」を提供することができた。

さらに、病院スタッフから転帰を振り返って様々な意見が出たが、専従看護師がいることで否定的な意見も聞くことができたと考える。だからこそ、関わったスタッフが努力してきたことを明確に打ち出す必要があるということを学び、報告とした。

第8回愛知緩和医療研究会　名古屋　2017年12月9日

持続皮下インスリン療法導入時における勉強会の効果

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社会医療法人愛生会　総合上飯田第一病院

【目的】
当院では2017年1月より持続皮下インスリン注入療法（以下 CSII）を導入した。導入時、患者指導ができる看護師が担当病棟にはいなかった。CSII への理解を深め、実際の患者指導に生かせることを目標に、担当病棟の看護師を対象に勉強会を行った。行った勉強会の効果を検討したので報告する。
【方法】
1）対象：担当病棟看護師14名　2）勉強会担当：自院担当在宅医療部担当者及び糖尿病看護認定看護師　3）時間：1時間程度　4）使用媒体：インスリンポンプ入門ナビ及びデモ機 CSII導入前に勉強会を実施、CSII導入後、担当病棟看護師へアンケートを配布し記入とした。倫理的配慮として、アンケートは無記名とし個人は特定されないこと、回答に関わらず不利益を受けないことを説明し同意を得た。院内の倫理委員会へも報告の上承認を得た。
【結果】
アンケート回収数14名（有効回答率100%）。CSII に関する用語の質問6項目では、全てにおいて「言葉は聞いたことがある」0 ～ 1名（0 ～ 7%）、「知らなかった」13 ～ 14名（93 ～ 100%）であった。パンフレットの内容が読み取れない、操作が不慣れ、インスリンポンプを見るのが初めて、インスリンポンプを初めて触る、関連する用語が聞き慣れず意味も分からない、実際では間違えないか不安だったという回答であった。もう一度勉強会を希望するかの質問では8名（57%）が希望と回答、指導前にデモ機で練習したいとの意見も聞かれた。
【考察】
CSII導入前にデモ機を使用しての勉強会を開催したが、CSII に関する用語の理解ができていない看護師が殆どを占め、パンフレットの内容を理解した上でのデモ機の操作練習にはならなかったと考える。インスリンポンプを取り扱うことが初めてであった看護師にとって用語の解釈も難易度が高い。インスリンポンプの操作を繰り返し練習できる環境を整えることは勿論ではあるが、インスリンポンプに関連した用語の理解から勉強会を行っていくことが必要だったと考える。

発表　第22回日本糖尿病教育・看護学会学術集会　福岡
2017年9月17日

外来と病棟における連携したパスを導入して

原田洋子

社会医療法人愛生会総合上飯田第一病院

【はじめに】
急性期病院における在院日数の短縮は、病院の存続や質をも規定する指標になっている。短期間で患者の情報共有し質の高い医療を担保するにはクリニカルパス（以下 CP）は、重要な役割を担っている。そこで外来と病棟で連携し、患者の情報共有と医療の質が担保できる CP の作成に取り組んだ。
【作成】
外来と病棟が連携した CP を作成することで患者の情報共有と質の高い医療の提供ができることを目標に CP作成した。
【運用】
今まで CP使用する際、病棟のみの運用で外来の関わりが少なかった。しかし、外来・病棟で重複する業務を各部署が行うことなどの問題や病棟が入院前、退院後・外来が入院中の患者状況を把握する機会や情報共有をする場面が少なかった。
【考察】
当院では、システム上の問題により CP を紙カルテで運用している。そのため、短期間で CP が運用される場合には業務の効率化や患者状況の把握などが容易にしやすくなった。しかし、入院や退院後の外来受診までに期間を要する場合、CP の運用や保管方法などに問題が生じた。また、外来部門では CP に関わっていたスタッフが少なく CP の知識や運用の流れを理解するのに時間を費やし、運用までに時間が掛かった。しかし、今回外来部門を巻き込むことで CP の必要性を病院全体に周知することができ、CP の充実や活動が図りやすくなった。
【結論】
今回、症例数が少なく効果を得られるまでに至らなかった。また、CP が紙カルテでの運用のため、外来と病棟での運用に問題が生じる部分もあった。しかし、内容や運用を今後、検討・整理していき CP運用をしていくことで常に患者の情報共有と質の高い医療の担保ができ尚且つ業務の効率化が図れると考える。

発表　第18回　日本クリニカルパス学会学術集会　大阪国際会議場
2017年12月2日

集団生活が苦手な患者へのデイケア滞在時間延長への援助
—精神社会的発達を考慮して—

社会医療法人愛生会　総合上飯田第一病院　○亀井理帆
元愛生会看護専門学校　結城厚子

【はじめに】
精神科デイケアの治療的効果に関する統計的な研究報告は多い。精神看護学実習で受け持った統合失調症の患者は、入院中でありながらデイケアに参加する治療を受け、社会復帰を目指していた。しかし集団生活が苦手で、デイケアの治療効果をあげることができずにいた。八木氏は、統合失調症の患者は自我機能の脆弱性に起因しいきにくさを感じているとし、看護援助としては患者の埋もれていた力への『気づきや発見』をし、患者に積極的なプラスのフィードバックを返すことで患者は自信を回復し、社会適応へつながると述べている[1]。
デイケアからすぐに病棟に戻ってしまう患者に、デイケアに同行し滞在時間を延長するように働きかけ、またデイケアでの体験を肯定的にフィードバックを行った。その結果、滞在時間の延長だけでなく発言や行動も前向きになったため、ここに報告する。
【目的】
集団生活が苦手な統合失調症の A氏が、デイケア滞在時間が延長し、また発言や行動が変化した理由を明らかにする。
【方法】
1　実践期間：看護実践期間7日間
2　対象
A氏20代の女性で、幼少期よりおとなしくコミュニケーションが苦手で友人と遊んだ経験が少ない。中高生の部活は人との交流を避けるため美術部を選んだ。高校卒業後に就職するが、電話での対応ができないことと職場での対人交流ができず、試用期間に解雇され職を転々とした。この時期に統合失調症を発症し、薬物療法を行っていたが不眠、幻聴が続いた。幻聴は恐怖感を伴うもので、壁にぶつかったり、転倒転落したりする危険行動が認められ入院となった。恐怖感が強い時は看護師にお祓いを求め、看護師のお祓いのような動作を見て落ち着くことができた。
デイケアに通いながら地域で生活できることを目標に、入院中ではあるがデイケアに参加していた。しかし人混みが苦手で、10 ～ 15分程度しか滞在できない状態が続いていた。入院後およそ2年が経過していた。
3　看護の実際
1）長期目標：デイケア滞在ができるようになり、退院する。
2）看護問題：集団生活が苦手であることと、人混みでの強くなる幻聴からデイケアに短時間しかいられない。
3）看護計画
(1) デイケアに参加する前に、目標設定（滞在時間・活動内容）を一緒に行う。
(2) デイケアでは他者と関わる機会を見つけ、コミュニケーションを促す。上手くできない時は、相手の意図を伝えたり、会話を促したりし、会話をつなぐようにフォローする。
(3)「帰りたい」という発言があったら、もう少し頑張るように励ます。
(4) 病棟に戻ったら、フィードバックを行う。
①滞在時間については、達成感がもてるように一目で分かる「目標達成表」をグラフとし、色塗りをする。
②デイケアでできたことの感想を、語りながら振り返り用紙に記入してもらう。
③頑張りを認め、できたことは褒めて一緒に喜ぶ。（A氏の発達危機は「学童期」と推察したため）。
4　倫理的配慮
個人が特定できないよう、氏名などの記載に配慮し、発表終了時には速やかに資料を処分する。

【結果】
実施1日目、デイケア滞在の目標時間は60分と決め参加したが10分後に「疲れたので帰ります」と帰ろうとした。滞在を促しても5分後には帰ろうとした。何回か励ましながら目標時間まで滞在できた。振り返りでは目標達成したことに達成感を感じており、「明日は卓球の試合をしてみたい」や「時間を少しずつ伸ばしていきたい」と前向きな発言があった。
実施2日目、目標時間を70分とした。昨日 A氏が希望していた卓球の試合を利用者にアドバイスをもらいながら行った。A氏は言葉を発することはなかったが、頷いたりアドバイスを真剣な表情で聞いている姿があった。上手くサーブができ周りの利用者に拍手をもらうと、嬉しそうな表情を見せた。滞在時間は50分であった。フィードバックでは、滞在時間に焦点を当てず卓球ができたことを一緒に喜んだ。
実施3日目、目標は60分とした。デイケアで利用者の B氏に話しかけられると下を向いて黙ったままだった。仲介するとポツポツと応えていたが、途中で肩が上がり目線が下がり言葉が出てこなくなったため、B氏のそばを離れた。その後手工芸に参加したが、利用者が増えると「帰ります」と発言があった。滞在を促すと自ら「あと15分」と目標を決め、居続けた。この日は合計1時間55分滞在できた。滞在時間をグラフに記入すると「こんなに時間が経っていたなんて、すごい！」と発言した。一緒に手を叩き喜んだ。午後も自ら希望し、デイケアに参加した。
実施4日目、作業療法に1時間参加していたため、デイケアは午後からであった。目標を30分としたが、20分しかいられず残念がっていた。作業療法も足したら1時間20分であることを伝えると「次は90分頑張りたい」と前向きな発言があった。
実施5日目、目標は90分であった。B氏が話しかけてくれたが何も話さなかった。会話を促すと小さな声で目を見て話し始めた。午後は恐怖感を伴う幻聴があったが、看護師に「お祓い」をしてもらうと、デイケアに一人で参加できた。
実施6日目、前日は実習がなかったのでデイケアの参加状況を確認したかったが、聞くより先に「昨日はデイケアに35分行けました。卓球の試合をしてきました。」と報告してくれた。拍手をして褒めると喜んだ。A氏から「B さんとお友達になれるようにフォローしてください」と依頼があった。B氏にそのことを伝えると、「私も友達になりたかった」と言われ、二人で話始めた。B氏が会話を主導していたが、A氏から話しかける場面も見られた。A氏が上手く会話が進められないときは、仲介し会話を促進させ、目標の90分を過ごした。振り返りでは、自分から「(目標達成表に) 色ぬりします」「学生さんがいなくなっても B さんと友達として長く続けたい」と発言したため褒めた。
実施7日目、目標は90分とした。自分から B氏に「横いいですか？」と声をかけ、B氏と一緒に90分を過ごし、最後に B氏と握手をして病棟に戻った。実習最終日だったので、フィードバック後に頑張りを讃える賞状を渡すと「学生さんがいなくなっても一人で行けるように頑張りたいです」との発言があった。
【考察】
　中井は「人が自ら積極的に取り組む意欲を保つためには、目標をもつことが重要です。(中略) 人は自分の取り組むべき目標が明確にあると、それに向けて意欲をもつようになります。」[2] と述べている。目標が明確になる前は、苦痛を感じれば病棟に戻るという進歩のない日々であった。しかし、滞在時間や活動内容の目標を明確にしたことで帰りたいと思っても、励まされることで、目標を意識し意欲的になれた。
中井は「学習者が学習目標に到達するには、フィードバックが重要です。フィードバックとは、学習者の行動を観察して評価結果を返すことです。」[3] と述べている。振り返り用紙や「目標達成表 (グラフ)」を用いたことで、できたことを実感し、自信がもて、変化していく自分への期待感につながった。そのため自分から「○○してみたい」という言葉が聞かれるようになった。
A氏の実年齢は20代だが、精神社会的発達の視点から見ると学童期の発達危機の最中である。仕事が上手くできなかったのは、コミュニケーションが苦手で学童期に友達や仲間との遊びや競い合いがなく、社会性を獲得できなかったためと思われる。服部[4] は学童期の「学びと勤勉性」について、成果が上がることを実感すると大きな喜びと自信を感じ、また周囲の人の称賛も得られることを知り、さらに能力やエネルギーを学習に結集し勤勉になると述べている。成果を目に見える形にし、上手く出来た時は褒めた。そのことが A氏の自信と埋もれた力を引き出すエネルギーになり、一人でもデイケアに参加し、友達を作りたいという積極的な姿勢につながった。しばらくは学童期を想定した対応を続けることで、学童期の発達危機を克服し人格的活力「有能感」を獲得でき、社会復帰へつながると考える。
【結論】
1　滞在時間や活動内容の目標を明確にしたことで、目標を意識し意欲的になり、その結果滞在時間が延長した。
2　肯定的フィードバック (努力を認めたり、できたことを褒めること) によって、達成感を感じ、それが自信につながり埋もれた力を引き出すエネルギーとなり、発言や行動が積極的になった。
3　未発達である学童期を想定した関わりを周囲がすることで、「勤勉性」の獲得に動き出した。
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血液透析患者における身体機能の変化と関連する基礎データの検討

馬路祥子[1)]、桑原道生[1)]、山本彩乃[1)]、上田周平[1)]、長谷川祐太[2)]、澤田里美[3)]、加藤優[4)]、鈴木重行[5)]

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【目的】
近年、血液透析 (以下、HD) 患者に対する運動療法の効果が報告されているが、診療報酬上の問題等で積極的に介入できないことが課題である。その為、優先的に運動療法を行うべき患者の選択が重要となるが、基準は明確でない。今回、HD患者の身体機能の変化と関連する基礎データの検討を行った。
【方法】
当院関連施設のクリニックの慢性維持 HD患者33例に対して、握力、Weight Bearing Index (以下、WBI)、E-SAS (日本理学療法士協会) の休まず歩ける距離、転ばない自信を評価し、1年後に再評価した。各評価項目で維持増加した群 (以下、維持増加群) と低下した群 (以下、低下群) の2群に分け、基礎データを比較検討した。基礎データは、初回評価時に以下の項目を診療録より後方視的に収集した：年齢、性別、身長、体重、HD の原疾患、HD期間、合併症の有無 (心、脳血管、整形、末梢神経、肺疾患)、Geriatric Nutritional Risk Index、Cardio Thoracic Ratio (以下、CTR)、血液データ (TP、Hb、BUN、Cr、eGFR)。
【結果】
WBI の低下群は維持増加群と比較して、年齢、eGFR が高く、CTR、HD期間が低かった。また、HD期間と CTR には正の相関、WBI低下群の HD期間と eGFR に強い負の相関が認められた。さらに、WBI の1年後の変化に影響する因子は eGFR (オッズ比：4.7、p<0.05) が挙げられ (的中率72.7%)、カットオフ値は3.86 ml/min/1.73m^{2}を閾値とした場合、感度100%、特異度72% であった。その他の評価項目にて2群間で差を認めたのは、休まず歩ける距離で心疾患の有無のみであった。
【考察】
HD期間と身体機能には負の相関があるとの報告が散見されているが、WBI が1年後に低下する患者の特徴として年齢が高く、HD期間が短いことが挙げられた。また eGFR は HD期間や CTR と相関を認め、運動療法を行うべき患者選択にて基礎データ項目としての重要性が示唆された。
【倫理的配慮、説明と同意】
事前に研究内容について文書により説明を行い、同意を得られた患者を対象とした。

発表　第26回愛知県理学療法学術大会　名古屋　2017年3月5日

継続的な身体機能評価が血液透析患者に及ぼす影響について

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【背景・目的】
血液透析 (以下 HD) 患者の運動機能を筋力以外も含め包括的に評価した報告は限られており、またそれらの経時的変化を求めた報告は極めて少ない。そこで本研究では、筋力、パフォーマンス、自己効力感を継続的に評価・フィードバックし、さらにその結果から必要と判断した HD患者に運動指導を行い、どのような影響を及ぼすかを検討した。
【方法】
外来通院可能な HD患者33例に対し、握力、膝伸展筋力、Short Physical Performance Battery (以下 SPPB)、休まず歩ける距離、転ばない自信、疼痛の程度を評価し、その結果をもとに運動指導群21例、経過観察群12例に分類した。また、運動指導後の運動継続の有無で運動指導群を実施群8例、非実施群13例に分類し、半年後、1年後に各評価指標を評価し比較検討した。

【結果】
運動指導あり -非実施群と経過観察群は初回測定時と半年、1年後で膝伸展筋力が有意に増加した。その他の運動機能は各群において変化を認めなかったが、対象者全体では膝伸展筋力、SPPB が初回よりも半年、1年後に有意に増加した。また運動指導あり -実施群は他の2群と比較し、年齢が有意に高値であった。
【考察】
本研究ではどの群においても運動機能の低下を認めなかった。定期的に運動機能の評価・フィードバックを行うことで、下肢筋力やパフォーマンスの向上、また高齢の場合でも運動機能の維持が可能であることが示唆された。

発表　第7回　日本腎臓リハビリテーション学会学術集会　筑波
2017年2月18日

大腿骨近位部骨折患者の術前栄養状態と術後嚥下機能の関連性の検討

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【目的】
大腿骨近位部骨折の術後に嚥下障害を発症もしくは悪化させる症例は少なくない。今回我々は大腿骨近位部骨折の術後に嚥下障害を呈した症例について、言語聴覚士（以下、ST）が嚥下障害を呈し介入した群と嚥下障害を呈さず ST が介入しなかった群に分けて、Geriatric Nutritional Risk Index (以下、GNRI）を含めた栄養状態等を評価し、術前栄養状態と術後嚥下機能の関連性について検討したので報告する。
【方法】
対象は2014年4月～ 2016年3月までに当院整形外科に入院した症例で大腿骨近位部骨折の術後に ST が介入した群：17名（男性5名、女性12名平均年齢87.4±4.3歳）と ST が介入しなかった群：20名（男性4名、女性16名平均年齢84.8±5.7歳）とした。ST の介入の有無を従属変数とし、性別、年齢、入院時 Barthel Index、術式、アルブミン、GNRI、体重、BUN、Na、Cl を調査した。各項目を独立変数とした多重ロジスティック回帰分析を行い、また、採択された結果より、ST介入を判別する閾値についても検討した。なお、多重曲線性の問題を回避するため独立変数間の相関の有無を検討し、互いに強い相関を有する独立変数が存在した場合はどちらか一方を削除した。
【結果】
嚥下障害の出現に影響する変数として GNRI のみが選択された（モデル $\chi 2$ 検定で $p>0.01$）. GNRI のオッズ比は1.15 (95%信頼区間1.03 ～ 1.27) であった。カットオフ値は91.03 (感度75% 特異度76%) であった。ROC 曲線下面積は0.76 であった。
【考察及び結論】
大腿骨近位部骨折術後の患者において、運動リハビリテーションのみでなく、栄養状態のアセスメント及び栄養療法、嚥下機能の評価も重要であり、その指標には GNRI が有用である可能性が示唆された。

発表　第32回日本静脈経腸栄養学会　岡山　2017年2月23日～ 2月24日

1年以内に再入院となった脊椎圧迫骨折患者の因子の検討

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【はじめに、目的】
高齢者において、脊椎圧迫骨折は頻度の高い骨折であり、80歳以上の43%が受傷しているという報告もある。また、脊椎圧迫骨折受傷をきっかけに、疼痛や脊椎変形により日常生活動作に制限が生じる高齢者も多く、入退院を繰り返す患者も少なくない。一方で、近年、脊椎圧迫骨折患者の歩行能力や在院日数についての報告は散見されるが、再入院となる患者についての報告は少ない。そこで今回、1年以内に再入院となった脊椎圧迫骨折患者の因子について検討したので報告する。
【方法】
対象は、2011年1月～ 2016年6月に脊椎圧迫骨折を受傷した94例（男性5例、女性89例、平均年齢81.9歳）とし、1年以内に脊椎圧迫骨折が誘因で再入院した群（以下、再入院群）と再入院しなかった群（以下、control 群）に分類し、再入院に影響する因子について比較検討した。検討項目は全て初回入院時のデータとし、入院時 Body Mass Index (以下、BMI)、Geriatric Nutritional Risk Index (以下、GNRI)、受傷機転、受傷部位、骨粗鬆症・認知症の有無、臥床期間、在院日数、Barthel Index (以下、BI) 改善度（最終 BI－初期 BI)、退院時歩行能力とした。従属変数を再入院の有無、調査項目を説明変数として多重ロジスティック回帰分析 (変数増減法) を行った。尚、統計学的有意水準は危険率5%未満とした。
【結果】
再入院群／ control群の各項目の平均値は、入院時 BMI：20kg/m^2 ／ 22 kg/m^2、GNRI：95.0 ／ 99.5、臥床期間：3.9日 ／ 5.5日、在院日数：23.9日 ／ 30.9日、BI改善度：25.3点 ／ 20.0点、受傷機転：転倒15例、他27例／転倒26例、他26例、受傷部位：胸腰椎14例、腰椎22例、胸椎6例／胸腰椎24例、腰椎21例、胸椎7例、骨粗鬆症：有14例、無28例／有18例、無34例、認知症：有10例、無32例／有17例、無35例、退院時歩行能力：自立30例、見守り10例、介助2例／自立35例、見守り12例、介助5例であった。多重ロジスティック回帰分析の結果、再入院に影響する因子として、入院時 BMI (オッズ比：0.869、$p<0.05$)、受傷機転（オッズ比：2.976、$p<0.05$)、在院日数（オッズ比：0.956、$p<0.05$）があげられた（的中率71.7%)。
【結論】
今回、退院時の歩行能力が自立であっても、腰痛の再燃や圧潰の進行など様々な要因で再入院となるケースのリスク因子は、入院時 BMI が低値であり、受傷機転は転倒以外、在院日数は短いという結果に至った。入院早期よりリスク因子を把握することは、退院後を見据えたリハビリを行う上で重要な一助になることが考えられる。
【倫理的配慮、説明と同意】
本研究は、ヘルシンキ宣言に沿い、当院の学術研究に関する方針ならびにプライバシーポリシーを順守して行った。

発表　第52回日本理学療法学術大会　東京　2017年5月12日～ 14日

TKA術後患者における反重力トレッドミル（AlterG）歩行時の免荷量の検討

Consideration of tokka amount which is at the time of antigravity tread Mill (AlterG) walking in a patient after a TKA operation

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【目的】
TKA術後患者において Alter G (以下 AG) 歩行時の免荷量の違いが、その後の平地歩行に及ぼす影響について検討した。
【対象及び方法】
対象は当院で TKA を施行した2例とし、研究デザインは ABA´型シングルケーススタディを用いた。杖歩行が監視で可能となった翌日より、通常の理学療法後に AG歩行を10分施行した。AG の免荷量は A、A´期は50%、B期は25%とし、各4回施行した。AG歩行後に10m快適歩行時の速度、歩幅、NRS を測定し、各期の測定項目ごとに二分平均値法を用い算出した改善度を比較した。
【結果】
2例ともに快適歩行時の速度と歩幅の改善度は、B期と比較し A、A´期で大きかった。疼痛は A、A´期と B期において、免荷量による一定の見解はみられなかった。
【結論】
TKA術後で杖歩行が監視で可能になった患者の AG歩行においては免荷量を25%で実施するよりも、50%で実施する方が快適歩行時の歩幅が増大し、歩行速度が向上する可能性が示唆された。

発表　第9回日本関節鏡・膝・スポーツ整形外科学会　北海道
2017年6月22日～ 6月24日

大腿骨頸部骨折患者の認知機能と身体機能の関連の検討

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【目的】
今回我々は、渡邉ら（2016）の「大腿骨頚部骨折患者の転倒状況と認知機能における特徴の検討」に加え、入院中の認知機能の経過と身体機能との関係について調査した。
【対象と方法】
2015年12月～ 2016年9月に当院に入院した65歳以上の大腿骨頚部骨折患者で手術適応となった133名のうち、評価の実施が可能である者を対象とした。認知機能低下と判断した者は家族からの聴取も行った。評価は、術前と退院時に MMSE、GDS-15を施行、同時に病前と退院時の歩行能力を比較した。統計処理は R2.8.1を使用し、Mann-Whitney の U検定とカイ二乗検定を施行した（有意水準5%）。尚、対象者と家族には研究の旨と倫理的配慮を説明し、承諾を得ている。
【結果】
133名中30名（80.0±7.8歳、男性6名、女24名）の聴取が可能であった。術前の MMSE は23点以下16名、24点以上14名であった。計算の項目は両群ともに最も得点率が低く、時間・場所・計算・図形模写の項目で両群間に有意差を認めた。MMSE23点以下の群は、退院時に有意な得点の改善を認め、うち4名は24点以上となった。また、入院中に MMSE の維持・改善を認めた者は、病前の歩行能力を維持する傾向にあり、MMSE が低下した者の中に病前同様の歩行能力を獲得した者は認めなかった。術前の GDS-15においては、MMSE 23点以下の群の方が有意に高く、うつ傾向にあることが分かった。
【考察】
術前の MMSE の下位項目の得点率は前回発表と同様の結果であり、側頭葉や頭頂葉機能低下など転倒者特有の傾向を示した。また今回の結果より、大腿骨頚部骨折患者の病前歩行能力獲得には、入院中の認知機能維持が重要であることが示唆された。合田ら（2014）は、入院中にリハビリテーションを多く受け、移動能力が改善した患者では、認知機能が低下しにくいことを示しており、今回の結果に類似している。以上を踏まえ、大腿骨頚部骨折患者に対する作業療法について検討する。

発表　第7回認知症予防学会　岡山　2017年9月22日～ 9月24日

急性期病院における認知症予防としての集団音楽療法

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【目的】
認知症高齢者を対象とする音楽療法は多くの報告があり、BPSD への有効性は認められつつあるが、中核症状への効果は確立されていない。今回、我々は急性期病院にて集団音楽療法を実施し、認知機能正常患者の入院に伴う認知症予防と、認知症患者への補助的な音楽療法の活用の可能性が示唆されたため報告する。
【方法】
対象は60 ～ 90歳代の患者5名で、整形疾患4名、内科疾患1名であった。集団音楽療法を週2回各30分、計6回行い、開始前と終了後に MMSE-J、GDS-15、PGS、VI を実施した。倫理的配慮にて対象者とその家族に本研究の趣旨を説明し同意を得た。
【結果】
MMSE-J では、開始前は24点以上3名、23点以下2名、終了時に改善した者は3名、低下した者は2名であった。GDS-15では開始前は、うつ傾向が2名、終了時では1名であった。PGS、VI は維持または向上を認めた。
【考察】
集団音楽療法を実施した5名中3名は認知機能正常であり、今回の集団療法実施に伴い認知機能が維持できたと考える。しかし、2名においては認知機能が開始前より低下しており、集団療法では手助けを多く必要とした。この2名の認知機能向上は図れなかったが、集団療法への参加により入院中の意欲の維持･向上が得られ、作業療法を円滑に進める補助的効果があったと考える。GDS-15ではうつ傾向であった2名中1名が改善した。この1名は実施前より身体機能への不安が強く悲観的発言もあったが、徐々に身体機能向上し集団療法に意欲的に参加でき、自己効力感の向上に繋がったのではないかと考える。Wilson ら（2012）は高齢者の入院に伴い認知機能低下が加速すると報告しており、大杉ら（2017）は抑うつ傾向にある高齢者は認知機能が低下しやすいとも報告している。今回の集団療法により認知機能正常患者の入院に伴う認知症予防の効果が期待でき、また、心理面からも認知症の予防になったのではないかと考える。急性期病院という非日常的な環境における認知症予防として集団音楽療法の活用を今後も検討していきたい。

発表　第7回日本認知症予防学会学術集会　岡山
2017年9月22日－9月24日

大腿骨頚部骨折を呈した高齢者の在宅生活の現状

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【序論・目的】
後期高齢者の大腿骨頚部骨折後のリハビリテーションにおいて、独居であることが在宅復帰の遅延・阻害要因となる場合がある。また、独居高齢者の退院後の生活状況や QOL についての報告は少ない。今回、我々は大腿骨頚部骨折を呈した独居の後期高齢者が在宅復帰後に、ADL は退院時の状態が維持されたものの、QOL が低下した事例を経験したので、若干の考察を加えて報告する。
【方法】
事例は82歳女性。診断名は右大腿骨頚部骨折。既往歴は特になし。入院前は独居で ADL は自立しており、弟夫婦とクリーニング店を経営し、住居は店の2階部分であった。弟夫婦はその隣の家に住んでおり、非常時などは協力しながら生活していた。現病歴として、住居である2階から階段を降りた後に、小さな段差に躓き転倒し、手術目的にて当院に入院した。入院4日後に右大腿骨頚部骨折に対し骨接合術を施行。術後翌日から、PT では基本動作・歩行訓練を実施、OT では ADL訓練を中心に実施した。 なお、倫理的配慮にて、対象者とその家族に対し、本研究の趣旨を説明し、報告の同意を得た。
【結果】
入院3日後の MMSE の結果は26点であった。また受傷 BI は100点であった。術後翌日には一部介助で車椅子坐位まで可能となり、BI は15点であった。術後2週には、見守りにて杖歩行可能となり、BI は90点になった。術後9週で自宅退院となり、退院前の MMSE は28点、BI は100点で、歩行は独歩であった。退院時の QOL は、日本整形外科学会股関節疾患評価質問表（JHEQ）によれば『痛み VAS』0mm、『痛み』27/28点、『動作』18/28点、『メンタル』26/28点で、合計71/84点であった。退院1 ヶ月後に自宅訪問し、退院後の状態を評価した。MMSE は27点、BI は100点であり、退院時の ADL は維持されていた。しかし、JHEQ では、『痛み VAS』9mm、『痛み』22点、『動作』16点、『メンタル』27点で合計65点であり、退院時に比べて QOL の低下がみられた。状態が悪化した項目は、『痛み』の「動き出すときに股関節に痛みがある」「股関節の痛みのため力が入りにくいことがある」、『動作』の「床や畳から立ち上がることが困難である」「しゃがみこむことが困難である」の4項目であった。この4項目の詳細について、事例に質問したところ、持続的な痛みがあること、その理由として在宅生活における動作の負荷量が想定していたより高かったことや、PT や OT で実施していた痛みへのケアがないことが挙げられた。一方で、『メンタル』は維持されており、在宅生活には、ほぼ満足している様子であった。
【考察】
本事例は独居で高齢ではあるが、術後早期より ADL が自立し、ADL も QOL も良好な状態で退院した事例である。しかし、退院1 ヵ月後の QOL の評価によれば、入院中には経験しなかった動作を経験したことや、痛みに対するケアがないという理由で、QOL が低下していた。一方で、メンタルでは良好な状態が維持されていた。この結果から、短期的に見ても、大腿骨頚部骨折治療後の後期高齢者の QOL は変化する可能性があり、このような状態に適宜対処することが、機能的予後の悪化予防に役立つかもしれないと思われた。

発表　第51回日本作業療法学会　東京　2017年9月23日

当院における認知症カフェの取り組み

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【背景】
認知症カフェは、オレンジプランにより普及し始めている。その位置づけとして、認知症介護者の負担軽減、認知症初期集中支援チームによる早期診断・対応、認知症の人や家族が専門家と情報共有し理解し合う（厚生労働省、2012）と示している。しかし、認知症カフェの事例や認知症カフェ参加者の ADL・IADL についての報告は少ない。今回、我々は地域住民の ADL・IADL を調査し、生活支援の相談や認知症予防等の取り組みを行っているため報告する。
【方法】
H29年2月～ 6月までの認知症カフェ参加者51名を対象とした。介入後にアンケート（基本情報とカフェ内容についての質問）と Lawton&Brody の IADL尺度（以下 IADL尺度）を使用し、生活上での困難はあるかという内容を調査した。 尚、倫理的配慮にて対象者とその家族に本研究の趣旨を説明し、同意を得た。

【結果】
女性37名、男性14名。60代13名、70代17名、80代21名。アンケートより”生活上で困ったことはない”との回答が多いが、利用者同士の会話を聴取していると、[時間や約束事を忘れてしまう][屋外活動の困難][老々介護による漠然とした不安]等が聞かれていた。屋外活動の困難は、IADL尺度でも減点が多く、次いで金銭管理の項目で減点があった。
【考察】
屋外活動の困難は歩行・体力等の身体的側面と複雑な公共交通機関の理解度、計画性等の認知機能の低下が考えられた。アンケートへのフィードバックや経過報告ができるよう利用者には声掛けを行っているが、スタッフ数が少ないため、利用者間の関係が密になるよう支援方法を試行錯誤している。また、当カフェは家族参加者が少ないため、勉強会や啓発活動を行い、家族間でしか見られない苦労の聴取や負担軽減へ繋がる情報を提供し続けていく必要がある。地域住民にとっては、通うことに不安がない身近な情報共有の場の提供と、そこに OT が存在していることを周知してもらい、地域との連携や認知症予防を継続していきたい。

発表　第7回認知症予防学会　岡山　2017年9月22日～ 9月24日

血液透析患者においての身体機能と転倒自己効力感との関連性について

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キーワード：血液透析、身体機能、転倒自己効力感

【目的】
一般に、地域高齢者は身体機能が低いほど転倒自己効力感が低く、活動範囲が狭くなる事が明らかとなっている。一方、血液透析（以下、HD）患者は、週に3日間の通院による時間的制約や疲労による不活動、合併症などの要因で非 HD高齢者と比較して身体機能が低下しており、社会参加や活動範囲は制限されている。これまで HD患者の身体機能やそれに伴う活動性に関しての報告は散見されるものの、実際に身体機能に対して転倒自己効力感がどのように関連しているのかを検討した報告はない。そこで本研究では HD患者における身体機能と心理的要因である転倒自己効力感との関連性を検討する事を目的とした。
【方法】
対象は当院関連施設のクリニックに通院し、歩行の自立している HD患者51名（男性39名、女性12名、平均年齢65.9±10.1歳）とした。なお、対象者には事前に研究内容について文書による説明を行い、同意を得た。身体機能の測定項目は、筋力評価として握力と膝伸展筋力を、運動パフォーマンスとして Short Physical Performance Battery（以下、SPPB）を測定した。転倒自己効力感の指標は E-SAS の中の転ばない自信を用い、質問形式にて聴取した。統計解析は、Pearson と Spearman の相関係数を用い検討した。なお有意水準は5%とした。
【結果】
転ばない自信は膝伸展筋力（r=0.428，P<0.01）、SPPB（r=0.531，P<0.01）と有意な相関が認められた。また、膝伸展筋力は握力（r=0.495，P<0.01）、SPPB（r=0.382，P<0.01）と有意な相関を認めた。
【考察】
近年、HD患者の高齢化から QOL や ADL の向上に焦点が向けられており、HD患者における日常生活の活動範囲を維持していく事は重要となる。今回、HD患者の身体機能は転倒自己効力感との関連性が認められた。地域高齢者においては、転倒自己効力感が低いと自ら身体活動を制限することで廃用症候群を招きやすいといわれている。HD患者も同様に、不活動や合併症による身体機能の低下のみならず、転倒自己効力感が低いことでも活動範囲を制限し、さらに身体機能を低下させる悪循環にあると考えられる。したがって、転倒自己効力感が低い HD患者に対しては心理的要因に目を向けた介入が必要であり、経過的な身体機能の評価や身体機能に対するアプローチに加え、転倒自己効力感の指標を聴取する事の必要性が示唆された。今後は、実際の活動範囲を含めたさらなる調査・検討を行っていきたい。
【理学療法学研究としての意義】
転倒自己効力感の指標である転ばない自信は、臨床上容易に聴取可能な質問表であり、簡便に HD患者の身体機能を窺える1つの指標となる可能性が示された。

発表　第33回東海北陸理学療法学術大会　福井
2017年11月11日～ 11月12日

当院の地域包括ケア病棟で転倒を繰り返す患者の特徴

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【目的】
入院中の転倒には疾患、環境など様々な因子が影響を及ぼすと報告されているが、地域包括ケア病棟（以下、包括病棟）において転倒に関する報告は少ない。そこで、今回当院の包括病棟で転倒を繰り返す患者の特徴を把握することを目的に調査を行ったので報告する。
【方法】
対象は H26.10から H28.9までの包括病棟の転倒報告108件である（1回転倒42件、複数回転倒66件）。方法は当院で使用している転倒・転落アセスメントシートの項目と、患者のカルテより転倒に影響がありそうな項目、計58項目を使用し転倒した時点で当てはまる項目をチェックした。予測因子を各項目とし帰結評価を1回転倒と複数回転倒とした。これらの関係に χ^2検定を行い有意差の得られた予測因子を投入して多重ロジスティック回帰分析を行った。統計処理には R2.8.1を使用し、有意水準は p=0.05とした。
【結果】
χ^2検定において有意差を認めたものは9項目であった。その内容は1.下肢に麻痺がある2.移動に介助が必要である3.認知症の症状がある4.麻薬使用中である5.排泄に介助が必要である6.介助が必要なのに1人で動こうとする7.疼痛が強い8. パーキンソニズム・パーキンソン病がある9.抗パーキンソン薬を内服している、であった。多重ロジスティック回帰分析では、疼痛が強い（p<0.01）、介助が必要なのに1人で動こうとする（p<0.05）の2項目が複数回転倒の特徴として抽出された。それぞれのオッズ比は6.990、3.164であった。
【考察】
介助が必要なのに1人で動こうとするという項目は身体機能低下の問題と、自己認識力・安全管理能力の低下の問題を持ち合わせた評価であると考える。この項目があてはまる患者は、問題点が複数でかつ複雑に絡み合っているため、病棟スタッフがより患者の行動に注意を払う必要がある。スタッフ1人1人の意識を高めるほかにも、マットセンサーやクリップセンサーなどの道具を使用することで患者の自己行動を素早く察知することも対応策として考える。疼痛が強く転倒した患者はベッドサイドでの立ち上がりやトイレ動作中に転倒をしているものが目立った。動作が不安定な際に疼痛が生じたことでバランスを崩し転倒に至っていると考える。
【理学療法研究としての意義】
複数回転倒する可能性のある患者を1回目の転倒直後に把握し転倒対策を行えば、転倒件数の減少が期待できる。リハ専門職が上記の2項目を専門家の目線で評価し多職種に情報を伝達することは、転倒・転落件数減少の1つの対策になると考える。

発表　第33回東海北陸理学療法学術大会　福井
2017年11月11日～ 11月12日

当院の超音波　興味ある1例

発表者：間瀬実香
共同演者：窪田智行、雄谷純子、杉山悦子、後藤亜裕美、柳沢あやの、遠藤果歩、徳永真衣

所属：社会医療法人　愛生会　総合上飯田第一病院

【はじめに】
当院では、乳腺エコーを検査技師が実施しており2013年乳腺センターが設立されてからエコー件数が増加傾向にある。
技師が乳腺エコーを施行した中で興味深い症例を経験したので報告する。
【症例】
　症例は87才女性。2016年11月右乳房のしこりを自覚し近くのクリニックを受診した。
当月、精査目的のため当院を受診した。既往歴は糖尿病、高血圧、慢性心不全。家族歴は乳癌、卵巣癌は既往なし。
〈触診所見〉
右 C領域に3cm大の腫瘤を触知。
〈マンモグラフィ所見〉
右 U－ O に円形、境界明瞭平滑な高濃度の腫瘤を認める。背景が脂肪性のためカテゴリー 4とした。
〈超音波所見〉
右 C領域、10時方向に円形、境界一部不明瞭な嚢胞様腫瘤を認める。腫瘤内部に嚢胞壁を這うような不整形の充実性エコーを認める。前方境界線断裂、ハローは陰性。外側陰影は、はっきりしない。エラストスコア4。嚢胞内癌疑い、カテゴリー 4とした。
〈CT所見〉
超音波所見と同様の部位にリング状の造影効果を示す限局した腫瘤を認める。

〈細胞診所見〉
背景に多くの血液成分がみられ、二相性不明瞭な異型細胞を認める。変性が強く、核の不整、クロマチン増量も認め、乳管癌を疑う所見でカテゴリー4とした。
〈病理診断所見〉
右乳房部分切除＋センチネルリンパ節生検を実施。少量の DCIS成分と中央に嚢胞構造をつくり胞巣状に浸潤する扁平上皮癌の所見。ER＝0、PR＝0、HER2＝0、Ki-67＝15 ～ 20%。
【まとめ】
通常、乳癌のほとんどが乳管上皮細胞が癌化した腺癌で、ごくまれに扁平上皮癌が発生することがある。扁平上皮癌の超音波所見の特徴は、壊死による嚢胞性変化を伴うことが多く、比較的境界が明瞭な腫瘤のことが多い。また、境界部高エコー（ハロー）を伴わないことが多い。また、腫瘤が急速に増大することも特徴の1つである。
超音波で嚢胞性腫瘤を認めた場合は、腫瘤内部の状態を確認し扁平上皮癌の可能性を考えながら超音波を実施する必要があると経験した1例であった。

発表　第34回名北乳腺研究会　総合上飯田第一病院（開催地）
2017年2月18日

Relationship between contrast enhancement of basal ganglia perivascular space and endolymphatic hydrops (2nd report)

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Purpose : Previously, we had demonstrated that the signal intensity of the perivascular space (SI-PVS) in the basal ganglia is related to the endolymphatic hydrops (EH) , and presumed that the development of the EH might link the glymphatic function. However, the study is insufficient to support this hypothesis, because we did not have showed the relationship between the SI-PVS and its volume and the relationship between SI-PVS and SI of the cerebral cisterns. Therefore, we should examine their relationships.
Methods : In 20 patients with a suspicion of EH, a MR cisternography (MRC) and a heavily T2-weighted 3D-FLAIR sequence (hT2w-3D-FLAIR) were obtained at 4 hours after IV-Gd. MR imaging was performed on 3T MR unit. The PVS in the basal ganglia was segmented on MRC using a region-growing method. The PVS regions were copied and pasted onto the hT2w-3D-FLAIR. The volume of PVS (Vol-PVS) and SI-PVS was measured. And then, the circular ROIs of 3mm diameter were set within the bilateral ambient cistern on the MRC. The ROIs on the MRC were copied and pasted onto the hT2w-3D-FLAIR and the SI of ambient cistern (SI-Amb) was measured.
Result : There was no significant correlation between the measurements of the Vol-PVS and the SI-PVS (r=-0.399, P=0.081). There was a positive linear correlation between the measurements of the SI-Amb and the SI-PVS (r=0.655, P=0.002).
Conclusion : SI of PVS is not related to volume of PVS, instead SI of PVS is related to CSF enhancement. These results may help to unveil the mystery of the glymphatic system.

The 45th annual meeting of the Japanese Society for Magnetic Resonance in Medicine 2017, Tochigi, 16 Sep. 2017

Gd 静注 4 時間後の脳脊髄液の信号値の測定：Labbe 静脈周囲にみられる強い造影効果についての検討

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【目的】
Heavily T2 強調 3D-FLAIR（hT2-FL）は液体に混在する低濃度の Gd 対して非常に高感度である。これを用いた研究では Gd 静注後の遅延造影相において、血管周囲腔や脳脊髄液が造影されることが確認されている。当院では通常量 Gd 静注 4 時間後に hT2-FL を撮影し内リンパ水腫の評価を行っている。これらを観察する中で、我々は Labbe 静脈周囲に特に強い造影効果を認める症例をいくつか経験し、Gd が静脈から脳脊髄液に浸出する過程に Labbe 静脈が特に強く関与しているのではないかと考えた。
今回の目的は、Labbe 静脈周囲脳脊髄液の信号強度とその他の領域の脳脊髄液の信号強度とを比較することである。
【方法】
内リンパ水腫評価目的のため、通常量 Gd 静注 4 時間後に 3T MRI 装置を用いて MR cisternography（MRC）と hT2-FL の撮影が施行された 30 症例を対象とした。信号強度を測定する領域は血管周囲腔、迂回槽、浅中大脳静脈周囲、Labbe 静脈周囲の脳脊髄液とした。MRC上で region growing 法を用いて各領域を抽出した。その ROI を hT2-FL 上にコピー＆ペーストし、信号値を測定した。得られた各信号値間の有意差、相関の検定を行った。
【結果】
Labbe 静脈周囲の信号値は各領域の信号値に対し正の相関を示した（血管周囲腔に対し r=0.554、迂回槽に対し r=0.735、浅中大脳静脈に対し r=0.702）。 Labbe 静脈周囲の信号値は各領域に比べて有意に高い値を示した（P<0.05）。
【結論】
Labbe 静脈周囲の脳脊髄液は、他の領域の脳脊髄液より高い信号値を示した。Labbe 静脈は Gd が血液系から脳脊髄液系に移行する過程に関与している可能性が示唆された。

第45回　日本磁気共鳴医学会大会　宇都宮　2016年9月16日

当院におけるスボレキサントの使用状況について

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鈴木彩美[1]、中川由紀子[1]、加賀香織[1]、籾山智美[1]、兼子結衣[1]
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【はじめに】
スボレキサントは新規作用機序を持つ睡眠薬であり2014年に薬価収載され、当院では2016年4月用された。
【目的】
後期高齢者における使用後の情報を収集し、低栄養や生理機能の低下が薬剤の効果に与える影響を調べる事、併用薬の有無が効果に与える影響を調べる事を目的とし調査を行った。
【方法】
2016年4月から2017年2月までの期間で入院中にスボレキサントを処方されていた後期高齢者の患者を抽出し、睡眠状況をカルテより後ろ向きに調査した。それらの患者について、e-GFR、体表面積、BMI、年齢、性別、血清アルブミン値、傾眠のリスクのある薬剤の併用などが睡眠状況に影響を与えた可能性があるか、統計的に調査を行った。睡眠状況は、効果なし、コントロール良好、傾眠ありの3群に分けてそれぞれの群で上記の値に有意差があるか調査した。
【結果】
いずれの群においても有意な差は認められなかった。後期高齢者において、特定の生理機能の低下が臨床的な効果に影響を与えにくい可能性が考えられた。引き続き情報の集積が望まれる。

発表学会：医療薬学フォーラム2017
開催地：鹿児島（鹿児島市民文化ホール）
発表日時：2017年7月1日

高齢者せん妄の発症に関連するリスク因子の考察

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【目的】
せん妄発症機序として炎症性サイトカインであるインターロイキン（以下IL）の濃度上昇が関連している可能性が示唆されている。今回 IL の代替指標として CRP が使用可能か検証するため、当院において認知症サポートチームが介入した患者について調査を行った。
【方法】
2016年4月から2017年3月まで介入した患者のうち、主科が内科、外科、整形外科の患者を入院中のせん妄の有無にて各科で2群に分類した。年齢、性別、入院前からの継続服用薬剤の有無、入院時血清アルブミン、入院時 CRP について2群間で比較した。統計学手法は X^2検定、Mann-Whitney検定を用い、有意確立5% とした。
【結果】
整形外科での入院患者について、せん妄発症患者群の入院時 CRP は、未発症の患者群に対して有意に高値であった。内科・外科については2群間で差を認めなかった。継続服用有無の点で内科の2群間において差を認めた。整形外科・外科については2群間で差を認めなかった
【考察】
CRP は IL濃度上昇により産生が亢進するため、IL濃度の上昇を代替する指標となりえるのではないかと考えられた。整形外科疾患では骨折が大部分を占めており、短期間で骨折が改善することは無く炎症反応は入院後も継続していたと考えられた。そのため CRP高値は IL高値を意味し、せん妄発症群で CRP が有意に高かったと考えられた。しかし内科、外科疾患などにおいては、感染症治療などにより IL が短期間で低下する可能性もあると考えられた。しかし CRP は IL低下と同時には変動しない。そのため入院時CRP高値が必ずしも IL高値を意味しなかったためこのような結果に繋がったと考えられた。
【結語】
骨折などの整形外科疾患においては、CRP値がせん妄発症リスク評価の指標の一つとなる可能性が示唆された。

発表学会：第27回医療薬学会年会
開催地：千葉（幕張メッセ）
発表年月日：2017年11月5日

失語症患者の退院支援

○小林香帆　髙島ゆかり　佐藤顕世

上飯田リハビリテーション病院

キーワード：失語症　施設入所　退院支援

【はじめに】
　私が医療ソーシャルワーカー（以下､MSW とする）として入職してから、一年半が過ぎた。様々なケースを担当する中で失語症患者の退院支援において、失語症の理解の少なさや活用できる資源の少なさを実感した。本発表において、支援経過の振り返りと失語症患者の退院支援の質の向上について考察する。
【事例概要】
　患者は、60代男性、病名は脳梗塞で当院に入院した。右麻痺は極軽度で、入院時より独歩で ADL は自立していた。失語症は理解・表出ともに重度で他者とのコミュニケーションは困難であった。病棟生活では、テレビを見て過ごし、日々の日課は把握していた。独居で、家族はキーパーソンとなる兄夫婦と父がいる。定年退職後、現在は無職で、趣味のドライブや釣りをして過ごしていた。
【支援経過と結果】
入院時より随時面談を行い、退院後も、見守りやリハビリの継続が必要であると考え、介護保険を申請した。認定調査に、兄夫婦と MSW が同席し、生活上で支障となることを伝えた。リハビリではコミュニケーションの代償手段を検討したが、困難であった。
当初、要支援1の認定がおりたが、失語症の症状が適切に認定調査に反映されなかったことから、区分変更し、要介護2となった。安全に独居生活ができる方法を様々な関係機関に相談し、サービスの活用や、失語症の方がどのように生活しているか情報収集を行い、自宅退院を目指したが、サポートの少なさから断念し、施設入所することとなった。
患者は、経済面を心配しており、年金の範囲内で入所できる施設を希望された。施設選びをする中で、失語症患者を受け入れたことがなく、トラブルを招く恐れがあると､断られる施設もあった。しかし､他の施設に打診し、失語症でコミュニケーションがとり辛くとも、対応しますとの返答をいただき、施設退院となった。
【考察】
　本事例では、活用できる資源の少なさを実感した。失語症患者への見守りや安否確認は、患者の生活を守る手段の一つである。それをサービスで補えない部分は、家族が支援しなければならず、失語症により話が意図したように伝わらず理解できない場面も多く、互いのストレスや不安となってしまう。そのため、本事例のように、自宅退院を断念することも少なくない。
退院支援とは生活の再構築である。施設での生活がこの先どのようなものになっていくか、施設職員とも退院後の生活のイメージを共有することで、安心した生活の提供が可能となり、生活の再構築ができると考える。入院中に想定した課題を解決し、次の生活の場である施設で本人、家族の思いに応え、いかにその人らしい生活を送れるかを常に考えられるような支援を行っていきたい。

ターニングポイントに関わる退院支援

佐藤顕世　髙島ゆかり　小林香帆　伊東慶一

【はじめに】
診療報酬改定や国の政策、世間の動向の変化により､退院支援も多様化した。疾患により生活が一変する方も多く、自宅退院が困難で施設入所となる患者も少なくない。本研究では、当院から施設入所した患者の傾向を調査し、政策や動向と照合しながら退院支援のあり方について考察する。
【方法】
2013年4月1日～ 2016年3月31日までに入院した患者954名のうち、自宅以外に退院した患者234名を対象とした。転帰先を老人保健施設、有料老人ホーム等の居住系施設、特別養護老人ホーム、療養型病院に分類し、急性期、回復期への転院を除いた176名について自宅退院以外の要因を調査し、転帰先の傾向を考察した。
【結果】
自宅退院以外の患者の平均値として、入院時 FIM は54.9点、退院時 FIM は69.0点、FIMgain は14.2点、アウトカムは21.5点で介助量や改善度は低い傾向にあった。
【考察】
介助量が多いことだけでなく、介助量が少なくても介護者が不在等、様々な理由で施設入所となる症例もある。施設入所は身体的要因以外に家族や介護力不足等の社会的要因も影響があることが示唆された。
【結語】
我々は回復期での入院は、生活の再構築のためにあると考えており、人生のターニングポイントとなる。国の政策や動向から介護者が不在で施設入所の退院支援を余儀なくされる症例も増えることが予想されるため、MSW の関わりは大切である。

軽作業の繰り返しによる握力低下の要因

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【背景】
高頻度の軽作業に従事することは、握力低下や筋痛を招く。軽作業を模したリーチ把握動作をラットに繰り返すと、握力が低下するという報告が散見されるが、その要因は明らかではない。
【目的】
リーチ把握動作の繰り返しによる握力低下の要因について、筋痛と骨格筋の形態を調査した。
【方法】
実験は10週齢 SD系雌性ラットを用い、課題を行わない対照群（n＝19）と課題を行う課題群（n＝22）に分けた。課題はペレットへの前肢リーチ把握動作を4回 /分、2時間 /日、3日 /週、3または6週間行った。ラットは握力と前腕屈筋群の機械的痛覚閾値を毎週測定した。実験終了後、浅指屈筋を摘出し、相対筋重量、筋線維横断面積を測定した。さらに、浅指屈筋中の MuRF1、Atrogin-1、Beclin1、LC3、Atg5、p62を mRNA、タンパク質レベルで検出した。
【結果】
課題群の握力と痛覚閾値は、課題前と比較してそれぞれ課題開始2週後、3週後から低下した。課題群浅指屈筋の相対筋重量、筋線維横断面積は、対照群と比較して6週後で減少した。課題群は対照群と比較して、6週後にMuRF1、Beclin1、Atg5、p62の mRNA量、タンパク質量が高値であった。
【結論】
リーチ把握動作の継続による握力低下は、課題開始2週以降は筋痛が要因であり、6週後は筋痛に加え、骨格筋萎縮が要因であったと推察された。

発表　第21回　日本体力医学会東海地方会学術集会　名古屋
2017年3月19日（奨励賞受賞）

当院における実績指数の傾向と今後の課題

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【目的】
H28年度の診療報酬改訂において、回復期リハビリテーション病棟入院料にアウトカムの評価として「実績指数」が導入された。そこで本研究では導入された実績指数から見た当院の現状について報告する。
【対象および方法】
2016年4月1日以降に当院へ入院し、同年10月31日までに退院した患者のうち、Functional Independence Measure(機能的自立度評価法：以下FIM）や基本情報等のデータに欠損のない脳血管疾患72名、整形疾患68名、廃用症候群2名の計142名を対象とした。調査方法は、当院で作成している患者データを後方視的に確認し、疾患、性別、年齢、手術の有無等の患者データと、実績指数を始めとするデータとを比較した。
【結果】
実績指数を疾患別で分けると、整形疾患では36.18で、脳血管疾患では34.08であった。疾患別での大きな差は認められず、どちらとも実績指数の基準である27を上回っていた。
さらにそれぞれの疾患を男女別でみると、整形疾患の男性群は38.54、女性群35.68と差はなかったが、脳血管疾患の男性群は40.30、女性群は26.60であり、男性に対し女性の実績指数が低かった。さらに脳血管疾患でも病型別で見ると、脳梗塞は31.36、脳出血は48.71その他は28.54と、脳出血群で高い結果となった。
【考察・まとめ】
徳永らは脳卒中では年齢が上がるほど女性と脳梗塞の割合が増えると報告しているが、当院でも脳血管疾患で入院している女性の平均年齢が76.09歳と男性の平均の71.57歳と比較して高く、脳梗塞の割合が脳血管疾患全体60％を占めていることが脳血管疾患の女性群の実績指数を下げる要因になったと考えられる。
今回は導入されたばかりの実績指数を2016年の上半期のみで分析したが、より詳細な分析を行うために、今後も継続したデータの分析を続けていこうと思う。
【倫理的配慮、説明と同意】
入院時に包括的に同意を得た臨床データについて、個人情報を識別する情報を予め取り除き匿名化した上で、後方視的な集計と分析を行った。

発表　第26回愛知県理学療法学術大会　愛知県　2017年3月5日

携帯電話の使用が困難となった症例に対する作業療法の介入

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【はじめに】
　今回、携帯電話の使用が困難となった症例に対し、症状に合わせて環境設定や操作練習を行い、携帯電話の使用を再獲得したため報告する。
【対象】
　左後頭葉内側と視床に脳梗塞を認めた右利き70歳代男性。発症二ヶ月時は明らかな運動麻痺はなく、右上下肢表在覚軽度鈍麻と痺れ、右同名半盲を認めた。FIM96/126。 MMSE24/30、SLTA は音読や文字の読解、書字の誤りあり。失行はなかった。VPTA は視知覚の基本機能、物体・画像認知、相貌認知、色彩認知、視空間の認知と操作低下を認めた。色彩は近似の色相の混同があり、模写は描けるが時間がかかった。以上より、統合型視覚失認が疑われた。
【倫理的配慮】
　発表に際し、本人及び家族に同意を得た。
【携帯電話の操作】
　症例より、携帯電話の使用について希望あり、病前から使用している折り畳み式携帯電話で評価した。キーの数字の読むことは時間をかければできたが、電源キーと通話キーの識別、画面の連絡先を読むことが困難であった。また、発信に用いるキーの探索や選択が行えず、発信の手続きを進めることが困難であった。
【環境設定】
　本症例は、視覚失認によりキーや画面の文字の認知が難しいこと、適切なキーの探索や選択が難しいことが、携帯電話の使用を困難としていると考えられた。そのため、キーを認知しやすくするための目印として、電源キー・通話キーに赤・青の色テープを貼り付けた。また、操作を簡略化し、画面の読み取りを省略するため、OT が携帯電話に一度押せば連絡先が表示されるキー（以下、短縮キー）に家族・友人の電話番号を登録し、キー操作が少ない手続きで発信できる設定で練習を開始した。
【練習の経過】
　発症二ヶ月より、短縮キーで発信する練習を開始。最初は OT が声掛けをしながら症例の指を短縮キーへ誘導し、テープの色で電源キー・通話キーを識別する指示をして、指でなぞらせてキーの位置関係の学習を促した。介入二週間で声掛けなしで短縮キーから発信可能となった。
　介入三週目に画面の連絡先が時間をかければ読めるようになったため、十字キーを操作して電話帳から発信する練習を開始。最初は十字キーの操作と、画面の切り替えや画面内のカーソル移動の関連がわからなかったため、声掛けをしながら操作を誘導した。介入四週間で目印を外し、声掛けなしで電話帳から発信可能となった。
【最終評価】
　発症三ヶ月時で FIM104/126。SLTA は仮名の読み取り、VPTA は視知覚の基本機能、物体・画像認知、色彩認知、シンボル認知で正答率が向上した。
【考察】
　有効な感覚モダリティに合わせ、目印の使用、発信方法の工夫、触運動覚を利用して訓練したことが携帯電話の操作獲得に寄与したと考えられた。電話帳からの発信は、経過に合わせて練習を導入し、十字キー操作と画面上の動作の関連を学習できたため、再獲得に至ったと考える。

第17回　東海北陸作業療法学会　名古屋
2017年11月18日～ 11月19日

「ビデオフィードバックにより着衣動作能力に改善がみられた右半球損傷例」

Improved dressing ability by video feedback in a patient with right-brain damage.

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【はじめに】
今回、着衣動作の獲得に難渋した左片麻痺を呈した症例に対し、ビデオフィードバック（以下、VF）を用いた介入により、その動作の改善が得られたため報告する。
【対象】
右被殻出血を呈した70歳台右利き男性。発症後5 ヶ月時の身体機能所見は左片麻痺（Br.st上肢Ⅲ手指Ⅱ下肢Ⅲ）、左上下肢の表在・深部感覚低下、異常感覚を認めた。起居動作自立、歩行見守り、FIM98/127であった。神経心理学的所見は、MMSE30/30、BIT通常検査133/146、コース立方体組み合わせテスト IQ79であった。尚、発表に際し、症例に同意を得た。
【着衣障害の症状】
開き服では、手順の誤りなく行えた。かぶり服では、左手、右手の順で袖に腕を通し、最後に頭部を通す手順で実施できるも、完遂は困難であった。その原因として、「衣服のねじれに気付かないこと」や、「左上肢への袖通しが不十分であること」が動作遂行を妨げていた。また、本症例も着衣動作に対する困難さを認識しており、「着衣中に服の左右や裏表のほか、衣服と手の位置関係が分からなくなる」との訴えが聞かれたため、次の検査を実施した。
【着衣動作の神経心理学的検査】
井上ら（2006）の検査を行った。(1）検者が呼称した衣服の右または左の部位を指す課題と、(2）衣服と身体部位との位置関係を答える課題を実施した。課題には、提示刺激として、ワイシャツの写真と実物の2条件を採用し、衣服の正面または、背面を提示する条件と衣服の生地の表面または、裏面を提示する条件の組み合わせで、計8条件で検討した。検査結果の特徴として、呼称の課題では、衣服の提示が正面よりも背面条件において、そして、衣服の生地が表面より裏面条件において、誤りを多く認めた。一方、衣服と身体との位置関係を答える課題では、衣服の表面提示より裏面提示条件で誤りが多く認められた。全ての検査課題において、実物提示より写真提示条件で、そして、提示の向きは背面より正面条件で誤りが多く認められた。
【介入と経過】
検査結果より、服の左右や裏表、衣服と手の位置関係に混乱してしまうことが着衣動作を困難としている原因であると考えられた。そのため、衣服のタグなどを利用した左右や表裏の確認方法のほか、衣服の操作を含めた着衣動作の手順の学習および、衣服と手の位置関係についての確認を実施した。訓練中は、声かけでの誘導に加えて、鏡を用いて動作の確認と修正を促した。しかし、改善は得られなかったため、着衣動作の指導を目的に新たな介入方法として VF を試行した。VF では、ビデオの映像をもとに症例の呈した誤りを症例に説明してから、衣服を用いた着衣動作の手順の訓練を実施した。撮影環境は、症例の上半身全体が映るように、症例の左前上方からビデオカメラで定点撮影した。VF による症例の反応として、困難を呈した時の衣服と身体の位置関係が実際の動作中よりも理解できている様子が認められた。そして、1回目の VF介入後の着衣動作において、左側の袖通しが不十分であることに自ら気づくことができていた。VF介入開始3日目には、声かけや指差しなどの誘導で着衣することができた。
【考察】
先行研究として、Tham ら（1997）は VF により、患者に自身の障害の気づきを促し、半側空間無視患者の机上検査に改善が得られたことを報告している。本症例に VF試行後、衣服と身体の位置関係に理解が得られたこと

や着衣動作中に左袖への気づきがみられた。本症例においては、VF で着衣動作の誤りや衣服と身体の位置関係を確認することが、着衣動作中の身体や衣服の左側への注意の向上につながり、着衣動作の改善につながったのかもしれない。

キーワード：着衣障害　ビデオフィードバック　半側空間無視

胸髄硬膜動静脈瘻により不全対麻痺を呈した一症例への FES の使用

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【キーワード】
FES、不全対麻痺、胸髄硬膜動静脈瘻

【はじめに】
機能的電気刺激（Functional Electrical Stimulation:以下 FES）は痙縮筋の抑制・歩行の改善・背屈トルクの上昇などに効果的であり、リハビリテーションに付加的に電気刺激を加えることの有効性はエビデンスが構築されつつあるといわれている。ウォークエイド（以下 WA）は、患者の歩行パターンに合わせて腓骨神経を電気刺激して足関節背屈を促す FES装置である。
【目的】
両下肢随意運動困難な症例に WA を併用して促通を行ったことで随意性と歩行の改善を図ることができた症例を経験したため報告する。
【症例】
症例は胸髄硬膜動静脈瘻により、第12胸髄以下の不全対麻痺を呈した50歳代男性。脊髄損傷の神経学的および機能的国際評価表（以下 ASIA）の運動スコアは50/100、痛覚・触覚スコアは82/112、筋力は MMT両上肢5、体幹2、両下肢1、Hand-Held Dynamometer、（以下、HHD）では大腿四頭筋0/0、表在感覚は左下肢重度鈍麻、右下肢脱失、深部感覚は両下肢脱失であった。歩行は、両金属支柱付き長下肢装具にて平行棒内歩行片道を最大介助であった。
【経過】
WA を4 ～ 5回 /週、両大腿四頭筋にチルトテーブル30° 背臥位にて電気刺激と同時にスクワットを実施した。2か月継続した結果、ASIA の運動スコアは72/100、痛覚スコアは94/112、触覚スコアは109/112、筋力は HHD で大腿四頭筋4.6/4.9へと改善した。歩行は、両プラスチック短下肢装具装着しピックアップウォーカー歩行が50m見守りで可能となった。単純な電気刺激よりも随意運動をトリガーとして電気刺激の制御を行う FES のほうがより効果的であり、促通運動と持続的低周波電気刺激の同時併用療法は回復期の重度麻痺への有用性が確認されていると報告されている。本症例でも、FES の併用により随意運動を伴う促通運動を行ったことが、下肢の随意性の改善及び歩行能力が向上した一要因となったことが示唆された。
【倫理的配慮、説明と同意】
当院倫理委員会で承認され、ご本人様にも同意を得た。

発表　第26回愛知県理学療法学術大会　愛知県　2017年3月5日

回復期病棟入院中の ADL変化とその要因 ～ FIM gain入院期間後半の変化に着目して～

石黒祥太郎

【背景】
入院患者の運動 FIM gain を月毎に見ていくと、1か月目が最も大きくその後徐々に低下するのだが、脳血管疾患患者に限って5か月目に再び大きく上昇していた。
【目的】
この遅れて現れる FIM向上の要因を突き止めること。
【対象】
H28年3月以降に当院の回復期病棟へ入棟し退棟した脳血管疾患患者173名。
【方法】
全患者を control群とし、脳血管疾患再発を除いた群（①群）、骨折を除いた群（②群）、呼吸器感染症を除いた群（③群）の運動 FIM gain を月毎に control群と比較。
【結果】
　各期間の運動 FIM gain の比較において、①群も②群もほとんど変化は見られなかった（全ての期間で±4%未満）が、③群の4か月目で control群に比べて225%と大きくなり、5か月目で66%と、小さくなった。
【考察】
　呼吸器感染症の患者を除いたことで4か月目の運動 FIM gain が向上し、5か月目は低下した。このことは、呼吸器感染症の罹患が4か月目に伸びるべき運動 FIM を5か月目に遅らせていたことを示唆しており、回復期病棟において呼吸器感染症に罹患することが入院後半における運動 FIM の向上を妨げる最大の要因という結果だった。運動 FIM をスムーズに向上させるためには一般的に行われている疾病管理や安全対策に加え、感染対策にも重点を置いて取り組んでいく必要があるものと考える。

Post-stroke apathy and depression: the relationship between symptoms and the course of recovery

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Abstract
Patients after cerebrovascular diseases (CVD) often suffer from apathy and depression, which are called post-stroke apathy and depression respectively. Post-stroke apathy and depression cause functional disabilities in daily living along with the physical disabilities. It is important to find patients suspected to have apathy and depression and to provide intervention appropriate for their symptoms. However, apathy and depression have not been evaluated properly in the clinical course of CVD, and there has been little research regarding these symptoms after stroke. Moreover, the relationship between post-stroke apathy and depression is still unclear, and effective intervention for the patients has not been established.
The objectives in the present study were to clarify changes in apathy and depression and their relation to cognitive and daily function in patients during the recovery period after stroke. Forty-two participants with CVD were involved (29 males and 13 females, aged 69.1±12.4 (SD) years old). Participants were evaluated using the following: Apathy Scale (AS), Self-rating Depression Scale (SDS), Mini Mental State Examination (MMSE), Clinical Assessment for Attention (CAT), and Trail-Making-Test A, B (TMT-A, B). Quality of life (QOL) was evaluated by Stroke Specific Quality of Life Scale (SS-QOL). Functional status was assessed by the Functional Independence Measure (FIM). The relationship between apathy and depression scales and other scores at the beginning and end of rehabilitation during the recovery phase after stroke was examined.
The apathy of patients their admission for rehabilitation after CVD tended to remain until discharge. The incidence of apathy did not correlate with depression at admission in the patients, but it came to correlate with depression by the time of discharge. The patients with apathy after CVD suffered more from cognitive disturbance, attention and executive dysfunctions than those without apathy. The ADL score did not correlate with apathy or depression scores. The QOL score correlated with apathy and depression scores in the patients after CVD. Apathy and depression showed different relationships with cognitive and physical function during the recovery stage, when therapists mainly manage their activities in the hospital. Apathy and depression symptoms should be distinguished from each other, and should be properly evaluated to provide appropriate intervention for both physical and mental recovery after stroke.

Key Words : stroke, occupational therapy, motivation, depression, rehabilitation

BCAA飲料摂取による栄養状態・骨格筋量への効果について

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【背景・目的】
　回復期リハ病棟の低栄養患者は、全体の半数を占めると報告されている。その中でも栄養とリハビリの組み合わせにより筋力や骨格筋量が増加する

といわれている。そこで当院における低栄養患者に対する BCAA飲料による積極的な栄養管理の効果について検討した。

【方法】

対象は、平成27年6 ～ 11月までに当院回復期リハ病棟に2 ヶ月以上入院した患者111名のうち低栄養状態に該当した41名とした。病院食のみ摂取した対照群 (n＝20)、病院食に加え週4回 BCAA飲料 (リハたいむゼリー) を摂取した BCAA群（n＝21）に分けた。評価項目は、体重、下腿周囲径 (CC)、MNA-SF、血清アルブミン値（Alb)、運動 FIM とし、入退院時に評価、比較検討した。統計手法は2元配置分散分析を行った後、多重比較に Bonferroni法を用いた。各評価項目との相関関係は Spearman の順位相関係数を用いた。有意水準は0.05未満とした。

【結果】

退院時の BCAA群の CC は、入院時と比較し有意に増加した。対照群と BCAA群の MNA-SF、Alb、運動 FIM は、入院時と比較し退院時に各群で有意に増加したが2群間では差がなかった。その他は群間・群内に差がなかった。一方で入院中に体重減少した患者割合は、対照群50%、BCAA群19%であった。体重変化量は、エネルギー必要量の充足率（r=0.50）およびタンパク質必要量の充足率（r=0.36）と、CC変化量は、タンパク質必要量の充足率（r=0.38）とそれぞれ相関関係を認めた。

【考察】

低栄養患者に対する BCAA飲料による積極的な栄養管理は、骨格筋量増加を示唆したが、体重増加には至らなかった。しかし体重減少抑制の可能性はうかがわれた。低栄養患者であっても、エネルギー量を多く摂取したものは体重増加し、タンパク質量を多く摂取したものは骨格筋量増加が推察された。

回復期リハビリテーション病棟協会　第28回研究大会 in広島
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