

Time course changes of reactive oxygen metabolites (ROM) as a serum oxidative stress marker in patients after surgery for compression myelopathy: an observational study

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Disclosure of Conflict of Interest

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There is no COI to be disclosed
with any companies.

Background

We previously reported

- Serum oxidative stress (before surgery) increased in severity in acutely worsening myelopathy.
- Severe oxidative stress in acutely worsening myelopathy can influence neurological recovery after surgery.

(Takahashi H et al. BMC Musculoskeletal Disord 2019)

Does serum oxidative stress improve by surgery?

Purpose

To determine the time course changes of reactive oxygen metabolites (ROM) levels as one of the serum oxidative stress markers in patients with cervical compression myelopathy after surgery

Patients and Samples

- Period: April 2015 – October 2018

- 31 serum samples collected from patients who underwent surgery of cervical compression myelopathy during preoperative hematological examinations at our hospital

- Exclusion criteria:

 - Cervical spondylotic radiculopathy / amyotrophy

 - Complicated with rheumatoid arthritis / neurodegenerative disorders

 - Diagnosed as the double lesion like cervical and lumbar disorders

- This study was given approval by our university human ethics committee

- Informed consent was obtained from all patients

Patients and Samples

- We divided the patients into the 2 groups
- Acutely worsening symptoms (AM) group : 17 patients
- Chronic symptoms (CM) group: 14 patients
- Acutely worsening symptoms of myelopathy were defined as that in which the JOA score of patients decreased by 2 points or more during a recent 1-month period

(Sakuma T, Takahashi H, et al. Eur Spine J, 2012)

Measurement of serum oxidative stress markers

■ Reactive oxygen metabolites (ROM) test

(Fukui et al. Hypertens Res, 2011)

- Not measuring reactive oxygen species directly but detecting hydro-peroxide (metabolites).
- The normal level of ROM: < 300 (U.CARR)

Moderate oxidative stress: > 340 (U.CARR)

Severe oxidative stress: > 400 (U.CARR)

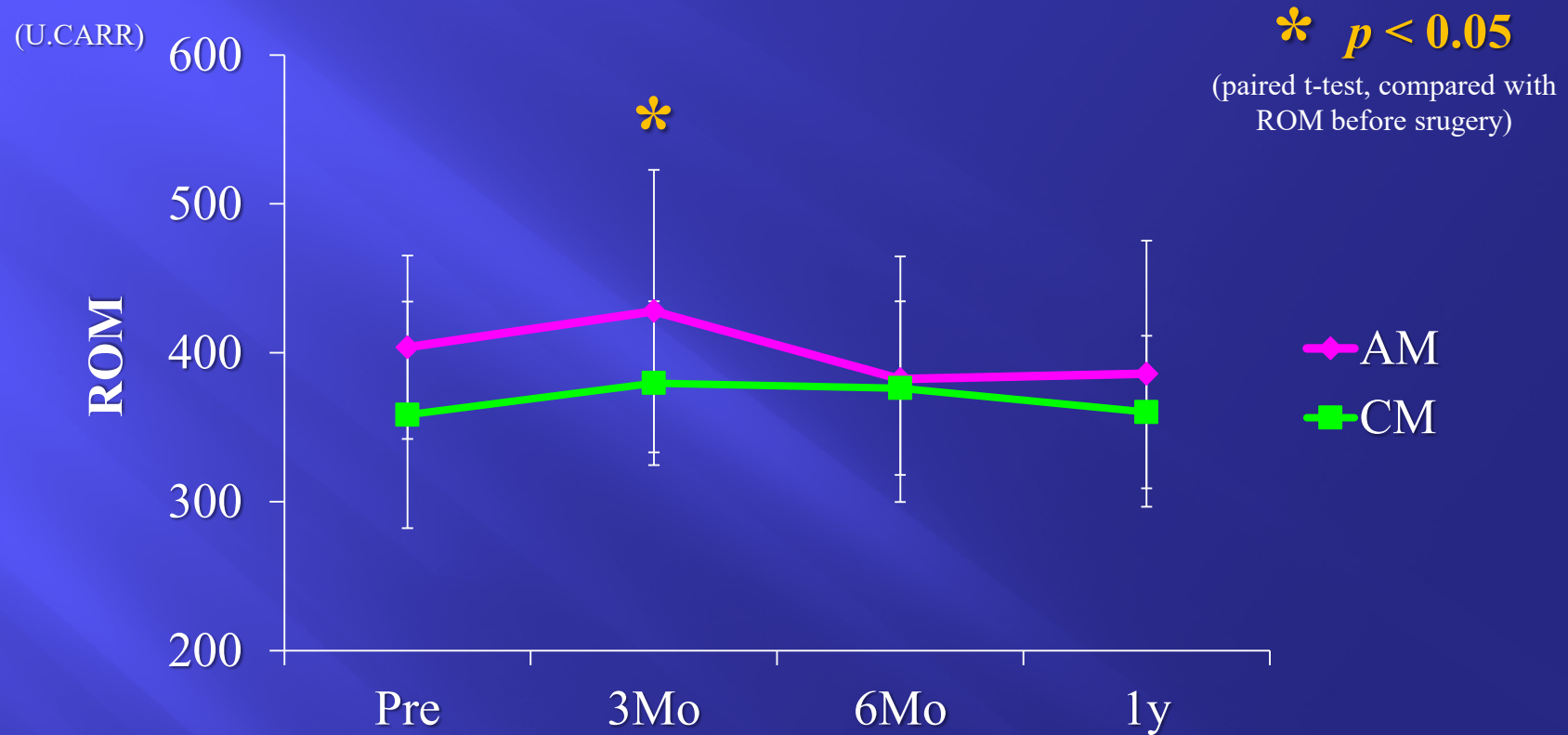
Outcome measure

- Time course changes of ROM in AM and CM
 - Before surgery, 3 months, 6 months, and 1 year after surgery
- Relationship between ROM and Sex, history of smoking, and diabetes
- Relationship between ROM and surgical procedure
- Neurological status
 - JOA score for cervical myelopathy (and the recovery rate)
 - Analysis divided into two groups: C5 palsy cases or not

Results: Patient Characteristics

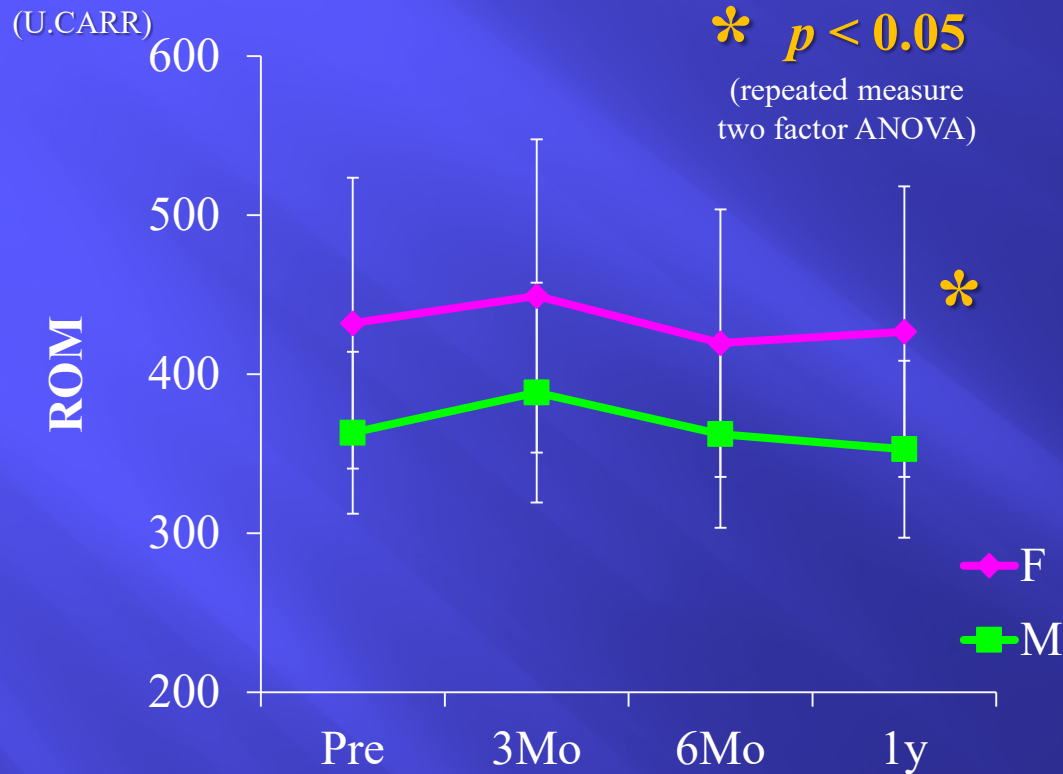
	AM	CM
Number of cases	17	14
Sex		
Male	11	11
Female	6	3
Age (years)	66.8 ± 9.8 (44-85)	69.2 ± 9.1 (49-79)
pre-JOA	10.6 ± 2.4 (5.5-14.5)	10.1 ± 3.1 (2.5-14)
Surgical procedure		
Anterior decompression and fusion (ADF)	12	8
Laminoplasty (LMP)	3	5
Posterior decompression and fusion (PDF)	2	1
C5 palsy	2/17 (LMP: 1 case, PDF: 1 case)	1/14 (ADF: 1 case)

Time course changes of ROM in AM and CM

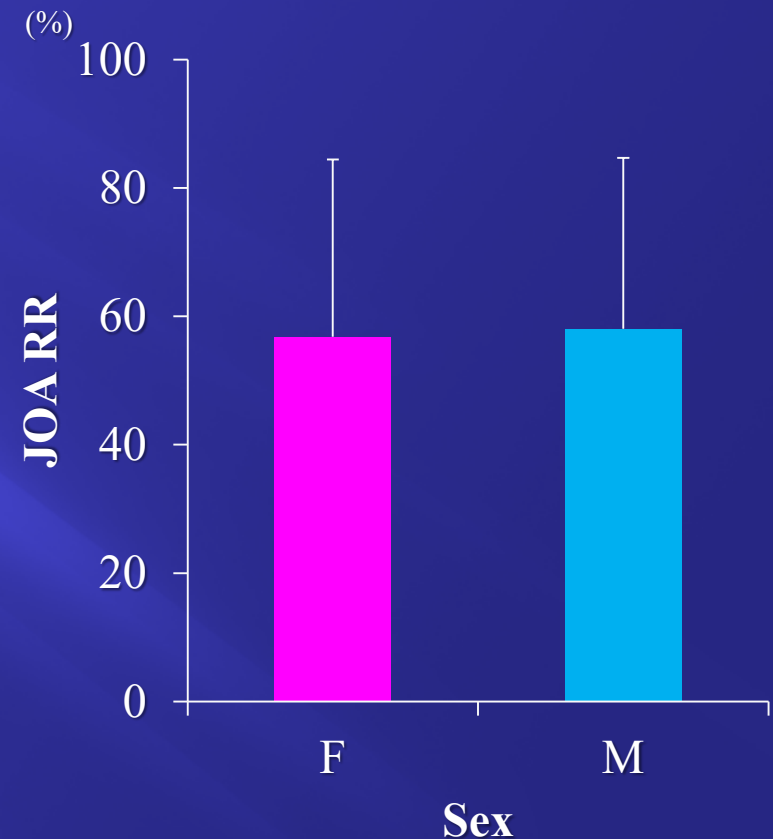


- ROM did not decrease but **increase** at **3 months** after surgery in both AM and CM groups ($p < 0.05$).
- ROM **decreased** at **6 months** after surgery and were maintained until 1-year follow-up.

Relationship between ROM and sex

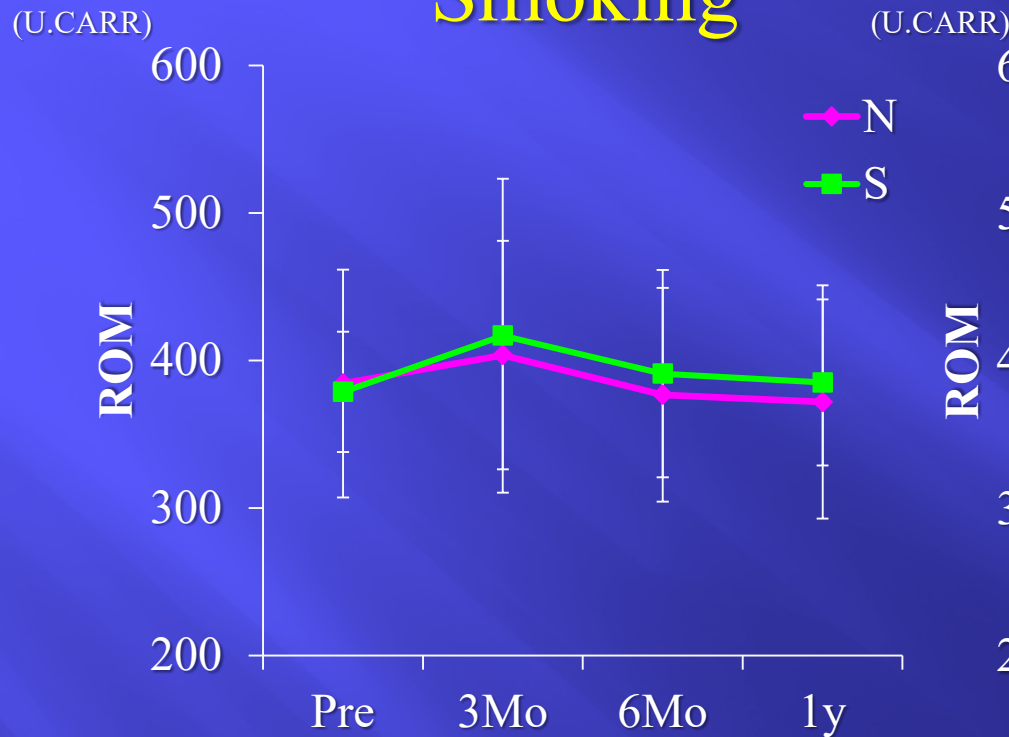


Recovery rate of JOA score and sex

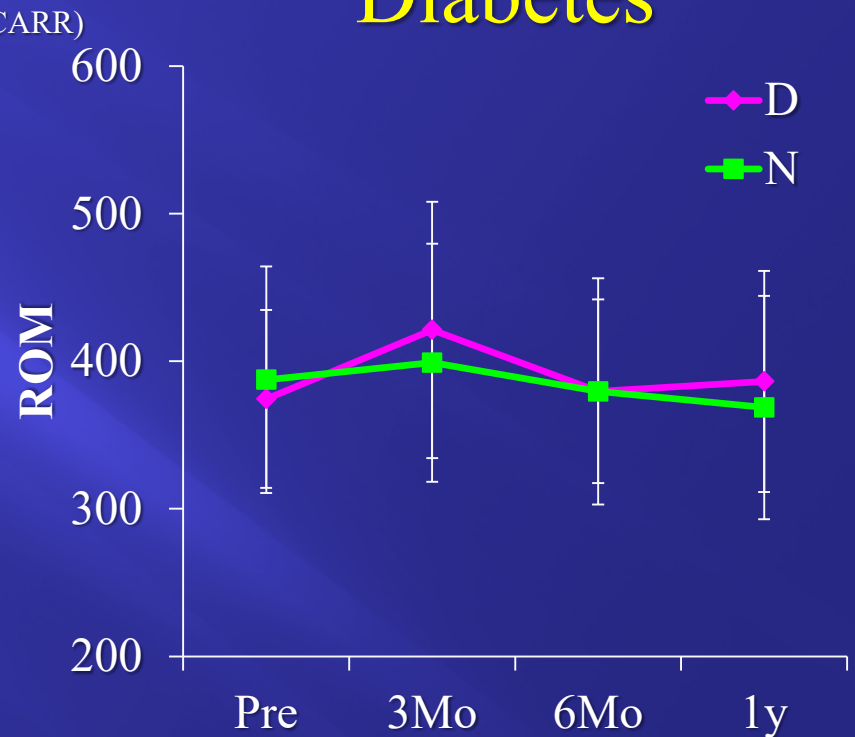


- ROM significantly increased in **female**.
- However, there was no significant difference between the recovery rate of JOA and sex.

Relationship between ROM and history of Smoking

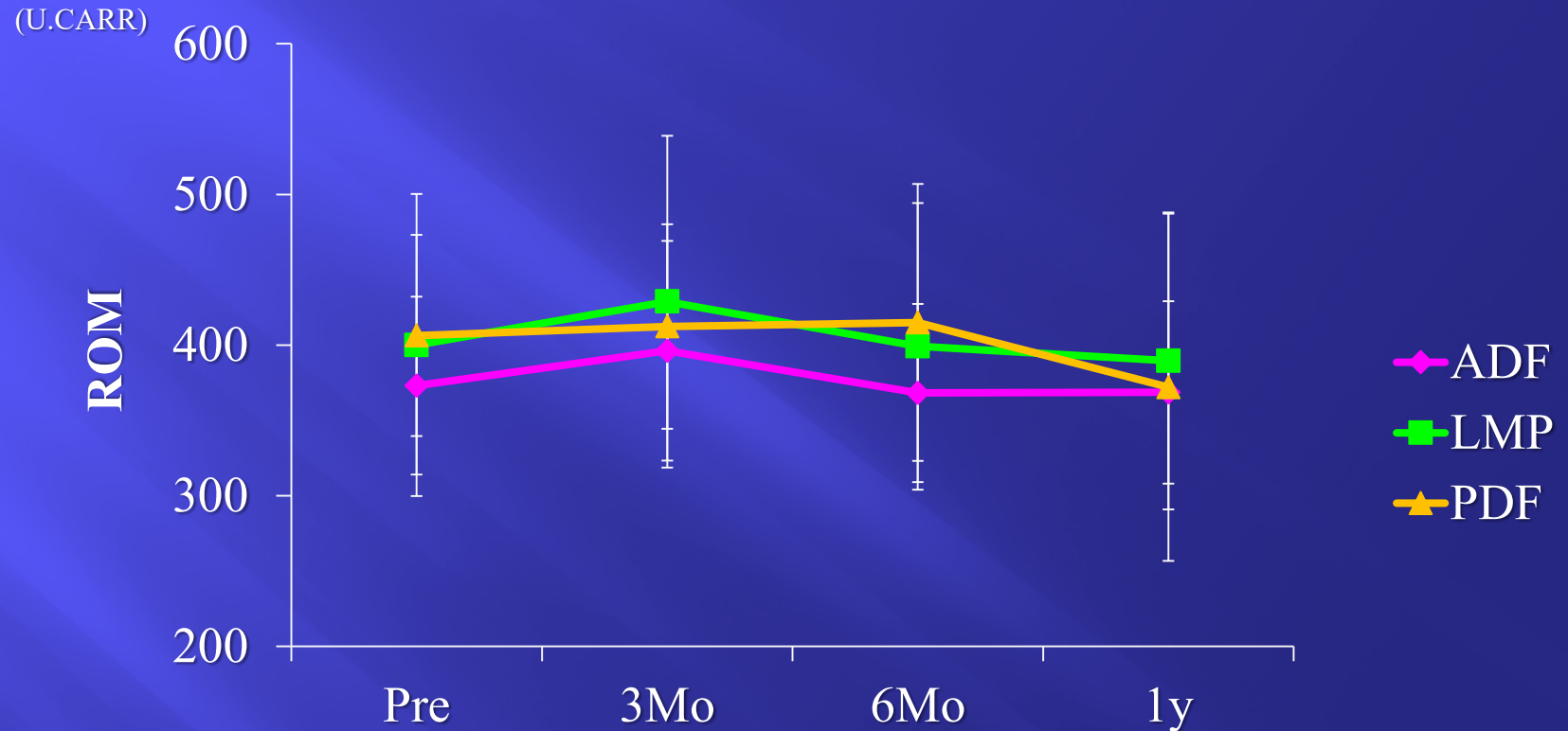


Diabetes



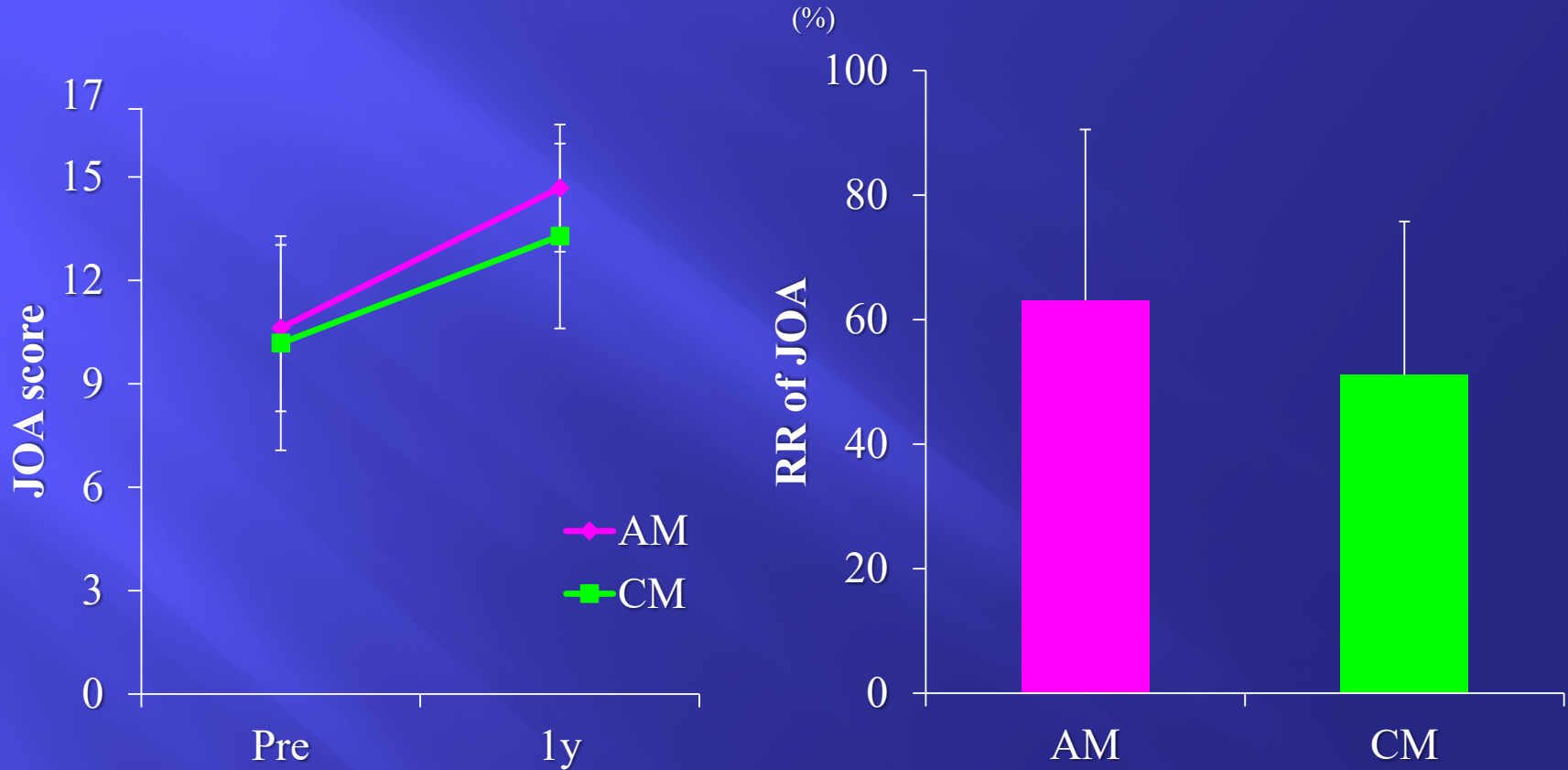
- There was no significant correlations between ROM and history of smoking or diabetes.

Relationship between ROM and surgical procedure



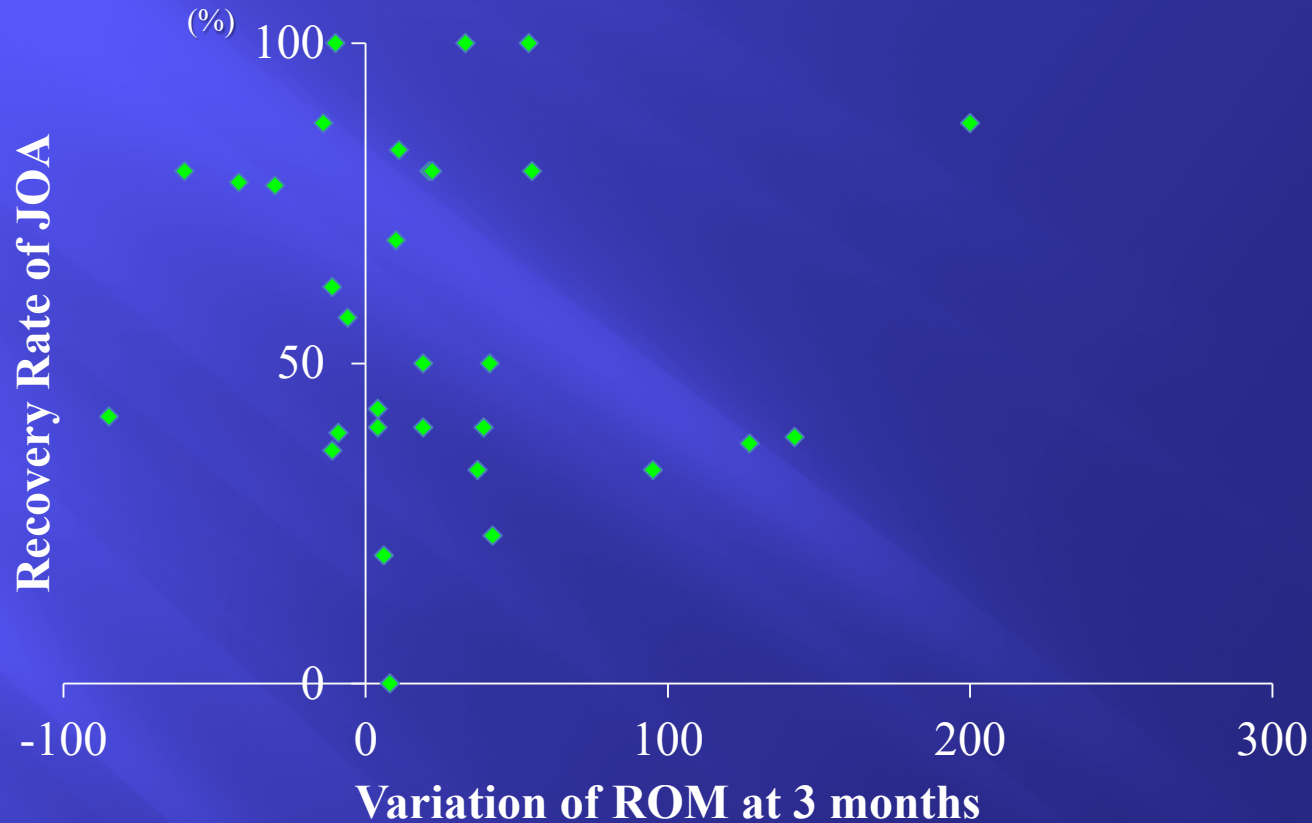
- There were no significant correlations between ROM and surgical procedures.

Improvement of JOA score in AM and CM



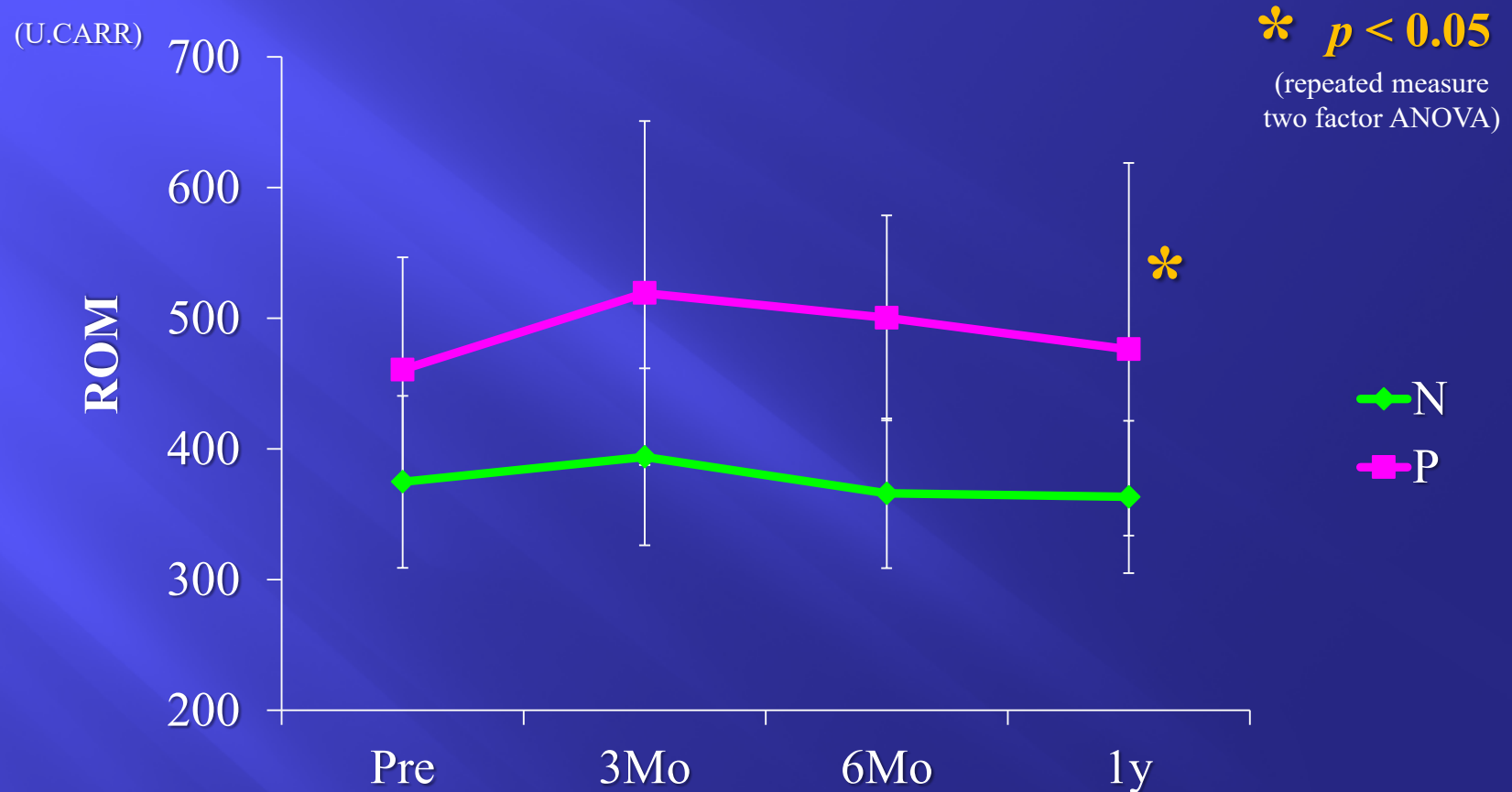
- Although slightly higher recovery rate of JOA score was seen in AM, there was no statistical difference in the recovery of JOA score between AM and CM.

Variation of ROM and recovery rate of JOA score



- There was no correlation between the variation of ROM at 3 months and recovery of JOA score.

Relationship between ROM and C5 palsy



- ROM complicated by C5 palsy were significantly higher than those in other cases
- The high ROM were maintained until 1-year follow-up.

Discussion

Oxidative stress and surgical invasion

In the cardiovascular field,

- Serum oxidative stress markers were elevated after surgery and **returned to normal values within a few days after surgery**

(Christen et al. Free Radic Biol Med, 2005)

- Serum oxidative stress markers **peaked 3 weeks after surgery**

(Kanaoka et al. Acuta Med Okayama, 2010)

In the present study, ROM did not decrease but **increase at 3 months** after surgery. We speculate the mechanism of this phenomenon:

- **Ischemia re-perfusion injury** after decompression of spinal cord

(Vidal et al, JCI insight, 2017)

- **Upregulation of endogenous antioxidants**

(Halliwell et al, Br J Clin Pharmacol, 2013)

Endogenous oxidative stress

Generally, serum oxidative stress increases in

- Elderly person
- Female
- Smoking
- Patients with diabetes

(Faienza et al. Horm Res Paediatr, 2012)
(Fukui et al. Hypertens Res, 2011)

Those reports have indicated that the endogenous oxidative stress is existing.

- In the present study, serum oxidative stress increased in female.

Neurogenic oxidative stress

On the other hands, serum oxidative stress also increases in

- Acute spinal cord injury
- Alzheimer disease
- Amyotrophic lateral sclerosis

(Nunomura et al. J Neuropathol Exp Neurol, 2006.)

(Wozniak et al. Oxid Med Cell Longev, 2012)

Those reports have indicated that the exogenous oxidative stress is existing that involved in neuronal cell apoptosis.

- In the present study, ROM significantly increased in cases complicated with C5 palsy.
- The neuronal apoptosis is more serious in cases complicated with C5 palsy.
- Elevated ROM may become one of the risk factors for C5 palsy.

Limitations

- Small sample size
- Bias in the degree of myelopathy and surgical procedure
- The detail mechanism of elevating the oxidative stress in compression myelopathy is unclear.
⇒ further clinical and basic research will be expected.

Conclusions

- Serum oxidative stress markers in compression myelopathy did not decrease but increased at 3 months after surgery despite the favorable neurological improvement observed.
- Serum oxidative stress markers were higher and remained elevated in cases complicated with C5 palsy.