

Paper 29

A possible cause of articular cartilage degeneration in the acute phase after anterior cruciate ligament reconstruction



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The authors declare that they have no competing interest.

Background

- **Intra-articular hemarthrosis** of injury knees contribute to the expression of various cytokines, which **leads to cartilage degeneration**. *(Jansen NW et al. Arthritis Rheum. 2007)*
- ACL injury is increased **risk for developing post-traumatic OA**. *(Louboutin H et al. Knee. 2009)*



Intra-articular hemarthrosis: POD4 after ACLR



37y, Men primary ACLR

**PO5Y (42y)
Developing OA after ACLR**

Purpose:

To evaluate the influence of intra-articular hemarthrosis on a disintegrin and metalloprotease with thrombospondin motifs (ADAMTS) and matrix metalloproteases (MMPs) activities in acute phase after ACLR.

Material & Method

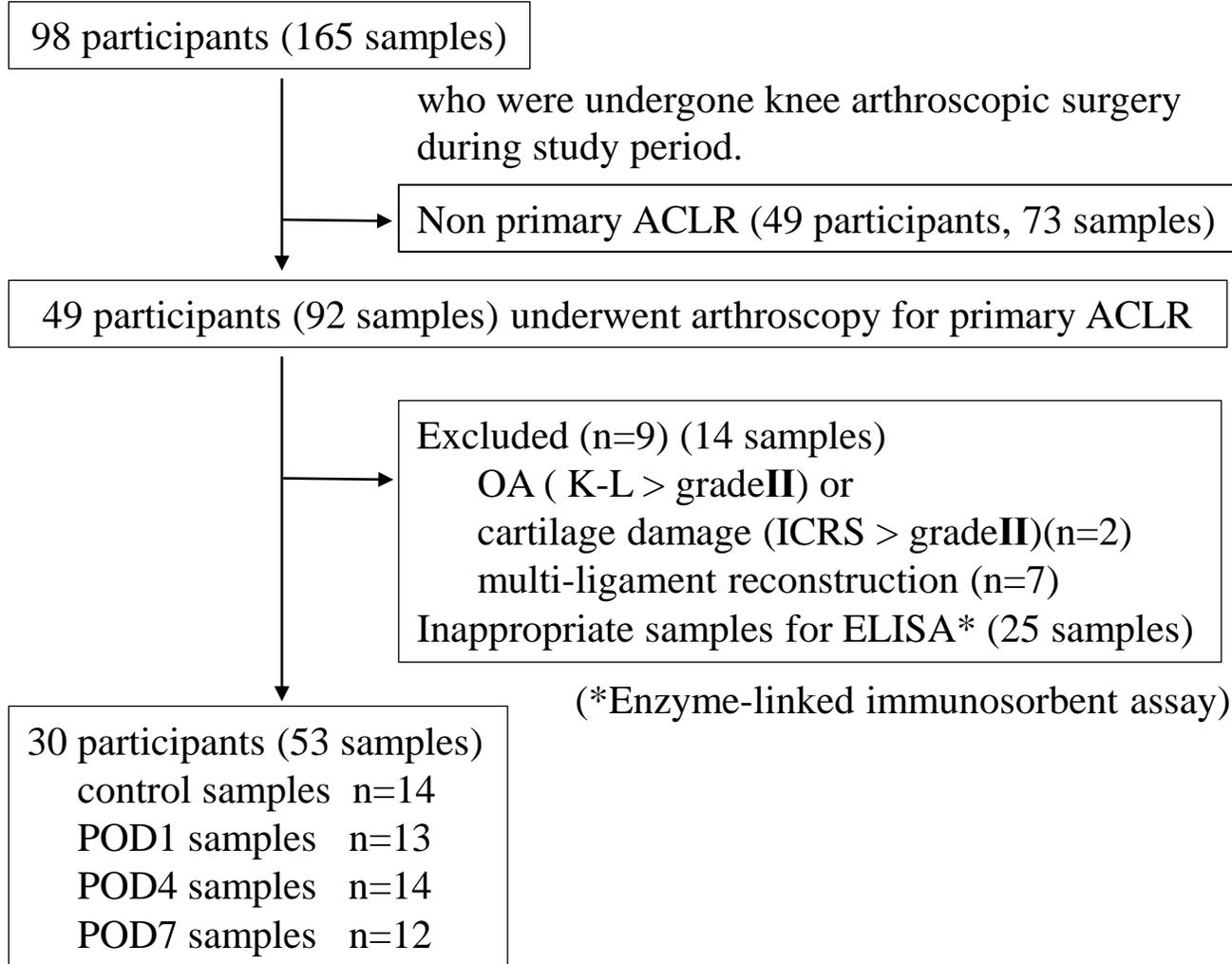


Figure 1 Flowchart of participant enrolment

POD4 and POD7 Samples were collected when postoperative joint effusion was observed.



POD1 samples were collected from drainage tube



POD4 and POD7 samples were collected by aspiration

Material & Method

➤ ELISA

- Five proteinases (**ADAMTS-4**, **-5**, and **-9** and **MMP-2**, and **-9**) were analyzed and were measured in intra-articular hemarthrosis and SF using a human ELISA kit.
(Cloud-Clone Corp., Katy, TX, USA, catalog numbers: ADAMTS4, SEK204Hu; ADAMTS5, SEK205Hu; ADAMTS9, SEK209Hu; MMP2, SEA100Hu; MMP9, SEA553Hu).

➤ Statistical evaluations

- Differences in levels of each proteinase among the four groups (control, POD1, POD4 and POD7) were compared by **one-way analysis of variance (ANOVA) with post hoc Tukey's honestly significant difference (HSD)**.
- **Chi-squared tests** were used for analysis of sex differences among the four groups.
- Differences in age, body mass index (BMI) and surgery time were compared by **one-way ANOVA with post hoc Tukey's HSD**.
- All computations relied on standard software (SPSS, IBM, Armonk, NY, USA).
- The level of significance was set at **$P < 0.05$** .

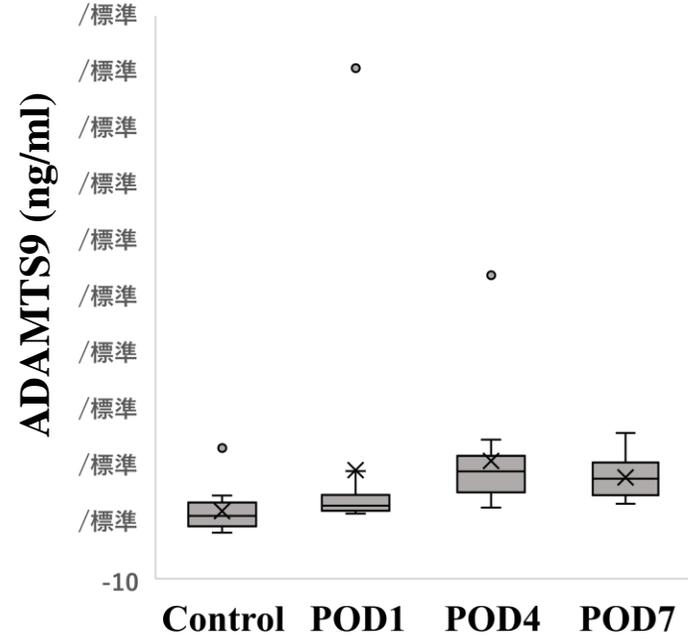
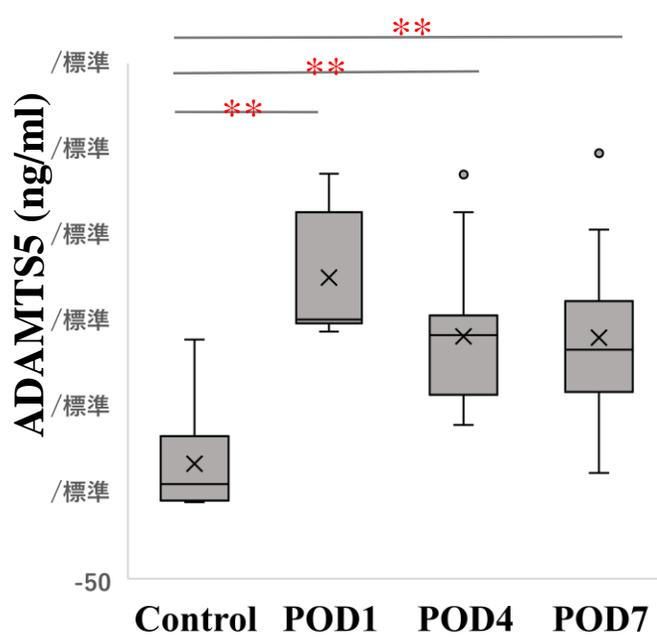
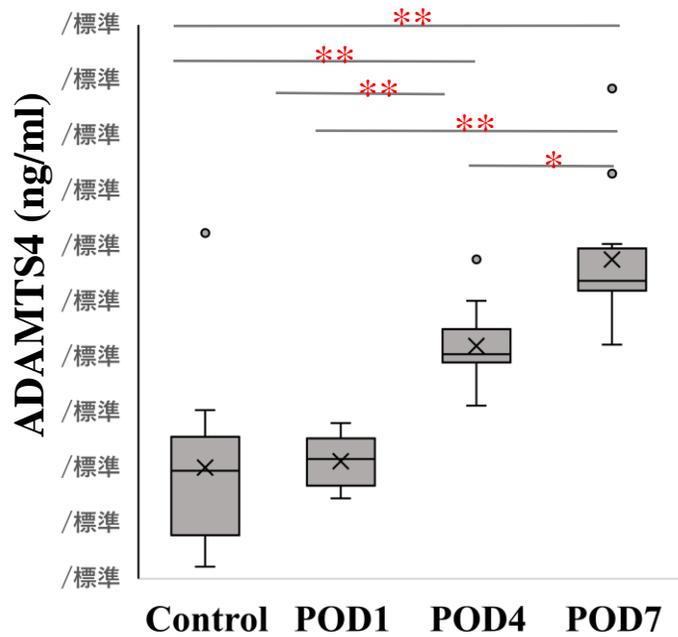
Result

		Control	POD1	POD4	POD7	p=value
Subject number		14	13	14	12	
Age (range; y)		27.4 ± 10.0	22.2 ± 7.1	30.4 ± 9.0	28.0 ± 7.7	0.113 ¹
Gender (male:female)		4:10	6:7	5:9	5:7	0.845 ²
BMI (kg/m ²)		23.0±3.9	24.3±3.8	22.9 ± 4.0	26.2 ± 7.4	0.310 ¹
Abbreviations: BMI; body mass index						
Note: values are expressed as mean ± standard deviation						
Statistics: ¹ one-way analysis of variance with post hoc Tukey HSD, ² Chi-squared tests						

Table 1 Characteristic of patients

※ Mean age, sex ratio, and BMI of groups have no significant differences between groups.

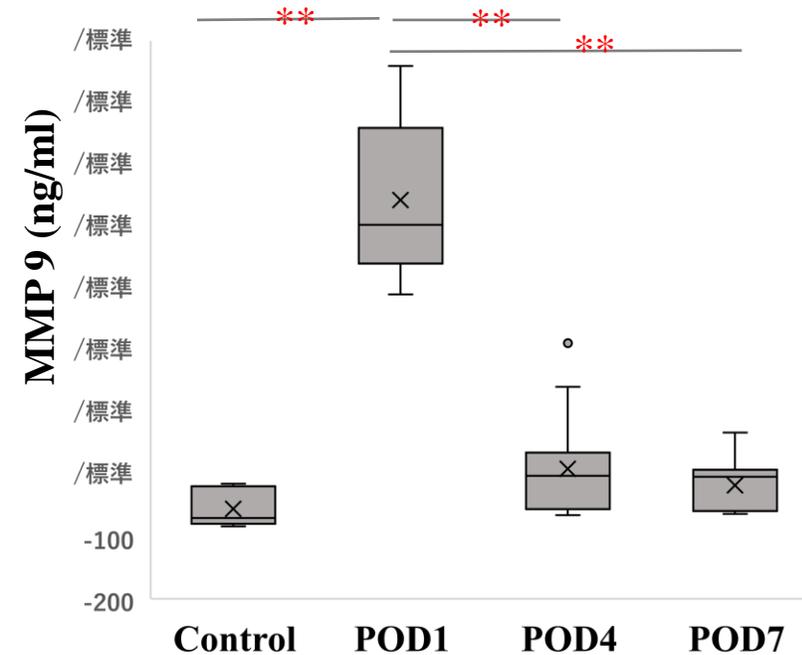
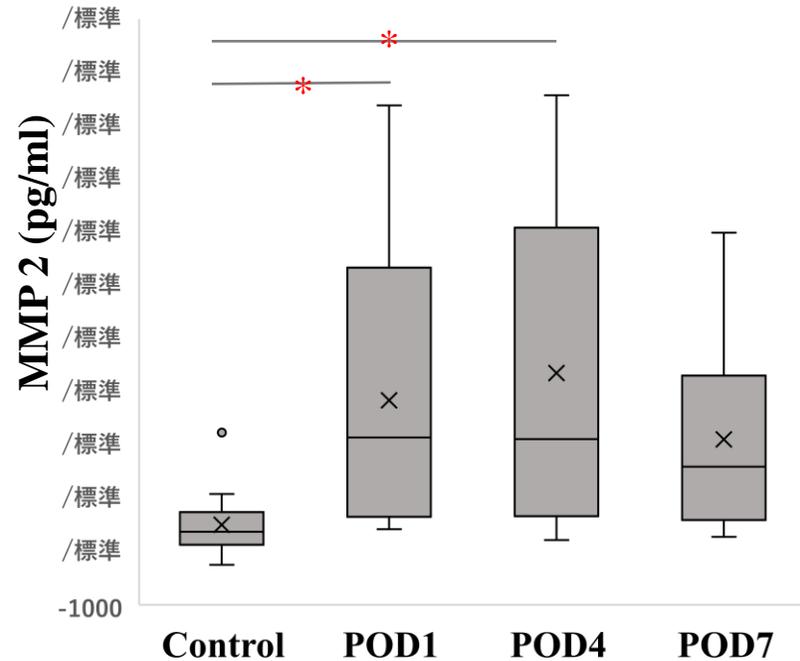
Result



(**<0.001, *<0.05)

- Expression levels of **ADAMTS-4** in **POD4** and **POD7** samples were **significantly higher** than in control and POD1 samples.
- Expression levels of **ADAMTS-5** in **POD1**, **POD4** and **POD7** samples were **significantly higher** than in control samples.
- Expression levels of **ADAMTS-9** did not differ significantly between samples

Result



(**<0.001, *<0.05)

- MMP-2 expression levels in **POD1** and **POD4** samples were **significantly increased** compared to control samples.
- Expression levels of **MMP-9** were increased only in **POD1** samples, **significantly higher** than in control samples.

Result

Time-Course study

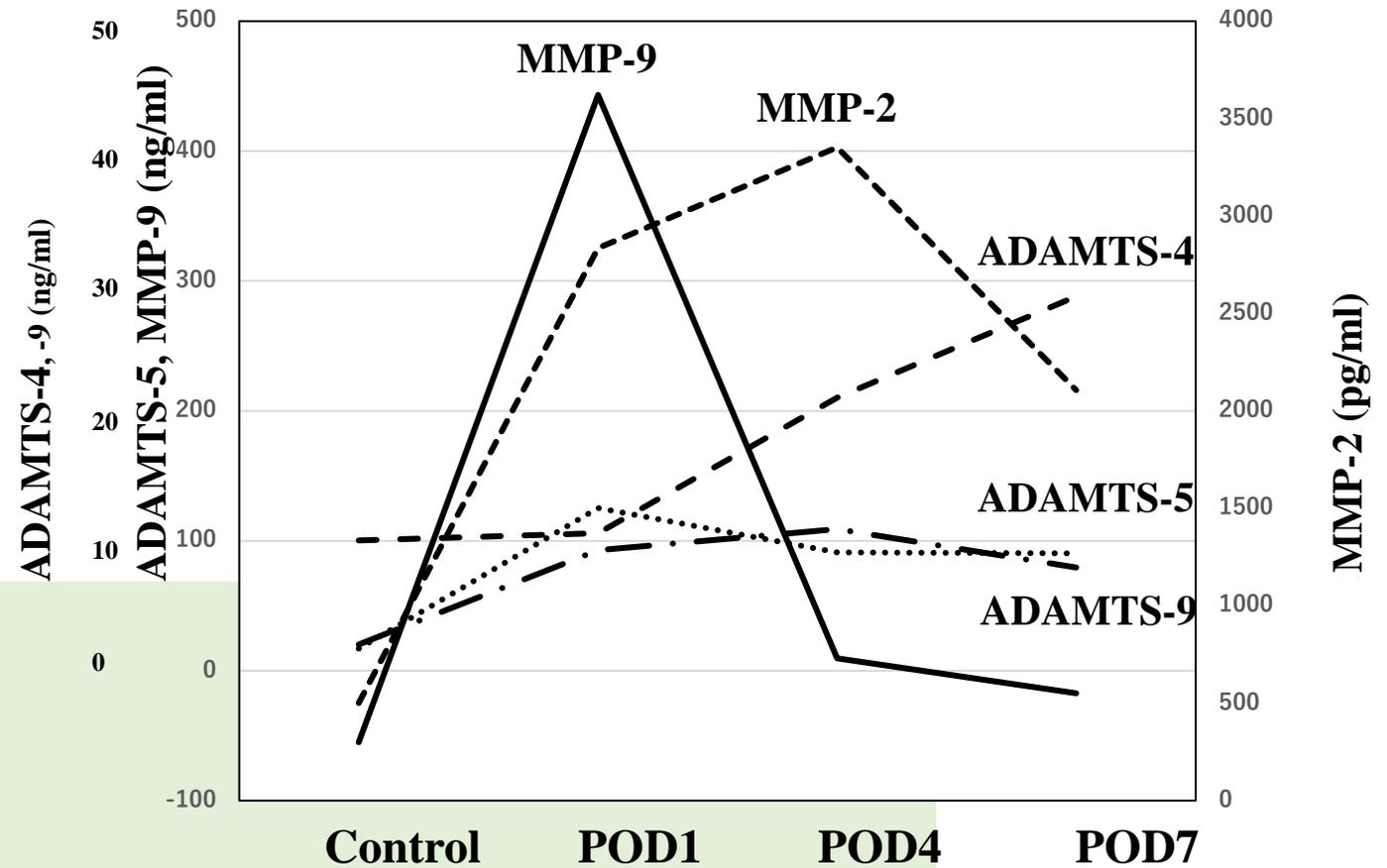
Expression levels of

ADAMTS-5 and MMP-9 peaked on **POD1**,

MMP-2 peaked on **POD1** and **POD4**,

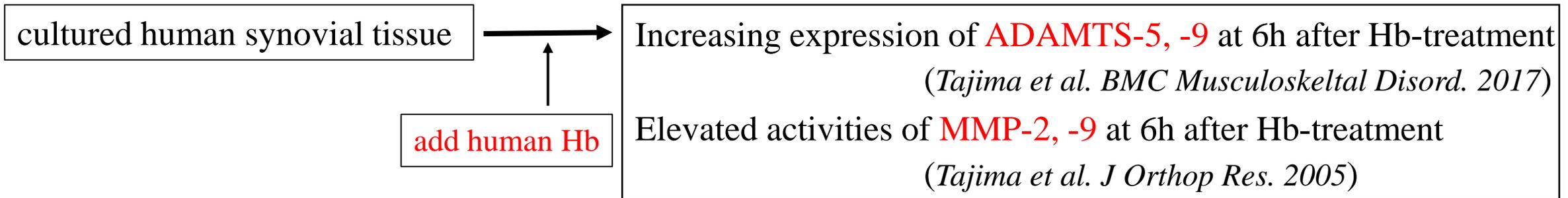
ADAMTS-4 **continued to increase within the study period** and thus peaked on **POD7**

ADAMTS-9 did not increase within the study period



Discussion

Previous in vitro study



This study

- **ADAMTS-4** and **-5** and **MMP-2** and **-9** are elevated in postoperative samples compared to control samples in **the acute phase** after ACLR.
- Aggrecan and collagen cleavage may be suggested to occur **within a day** after ACLR.
- The mechanism of this cartilage degeneration is thought to involve **Hb from intra-articular hemarthrosis** after ACLR.

Discussion

Study of cytokine levels after ACLR

	journal	year	Patient number	sample	target protease	post-operative time	control
<i>Zysk</i>	<i>KSSTA</i>	<i>2004</i>	13	SF	IL-6, BMP-2	7days	SF before surgery
<i>Akesen</i>	<i>Acta orthop Trauma Turc</i>	<i>2009</i>	16	SF	TIMP-1	18h	SF before surgery
<i>Hayward</i>	<i>KSSTA</i>	<i>2011</i>	14	SF	IL-1, IL-6	1h, 6h	SF before surgery

⇒ Inflammatory cytokines were increased in SF shortly after ACLR. That may contribute to cartilage degeneration.

The effect of **blood components** on cartilage damage (*Roosendaal et al. Arthritis Rheum. 1999*)

- whole blood or a combination of mononuclear cells and erythrocytes inhibit proteoglycan synthesis and diminish the content of proteoglycans in the cartilage matrix.
- ⇒ **Erythrocytes play an important role in blood induced cartilage degeneration.**
- ⇒ Immediate treatment for intra-articular hemarthrosis, such as aspiration or wash out, may be needed for prevention of OA.

Conclusion

- The expression of ADAMTS-4, -5 and MMP-2, -9 were elevated in acute phase after ACLR. These findings suggested that intra-articular hemarthrosis after ACLR may contribute to cartilage degeneration.