

1 **Title page**

2 **Running title:** Rheumatoid Arthritis and Hallux Valgus Surgery

3 **Title:** The Influence of Medial Cuneiform Inclination on Postoperative Hallux Valgus

4 Recurrence in Rheumatoid Arthritis Patients: Insights from the KURAMA Cohort Study

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Rheumatoid arthritis (RA) is an autoimmune disease that significantly impacts the quality of life and mobility due to chronic inflammation and joint damage (1, 2). Hallux valgus (HV), characterized by a misalignment of the first ray of the foot, is a common foot deformity in RA patients, causing pain and difficulty in wearing shoes (3). Among the myriad afflictions RA imposes, foot deformities rank prominently, with an estimated 90% of RA patients experiencing some form of foot deformity and a notable 25 to 40% undergoing surgery to address forefoot complications (3). Previous studies demonstrated that the instability of the first tarsometatarsal (TMT) joint can be related to HV deformity, and the presence of the instability may be predictable by assessing the articular facet of the medial cuneiform in plain anteroposterior X-rays (4-11). Surgical correction of HV includes various procedures, with joint-preserving techniques becoming more prevalent due to advancements in RA treatment (12). Recurrence of HV deformity is a known postoperative complication (13). However, no study has shown the association between HV recurrence and the inclination of the articular surface of the medial cuneiform. This study aims to assess the relationship between medial cuneiform morphology and HV recurrence after distal metatarsal osteotomy (DMO) in RA patients.

47 We retrospectively investigated RA patients who underwent DMO for
48 moderate to severe HV (defined as $HVA \geq 30^\circ$ (14)) between 2005 and 2022 and were
49 followed up more than 1 year using KURAMA (Kyoto University Rheumatoid Arthritis
50 Management Alliance) cohort (15). All patients fulfilled either the 1987 diagnostic
51 criteria of the American College of Rheumatology or the 2010 American College of
52 Rheumatology/European League Against Rheumatism classification criteria for RA (16,
53 17). Clinical data, including disease activity, medication usage, and foot function
54 scores, were collected. Standard weight-bearing foot X-rays were analyzed
55 preoperatively, postoperatively, and at follow-up visits. DMO was performed using
56 Hohmann osteotomy as described previously (18). Recurrence of HV was defined as
57 hallux valgus angle ($HVA \geq 20^\circ$ after surgery (3, 19). The morphology of the TMT
58 articular facet of the medial cuneiform was assessed by first TMT joint angle
59 (1TMTJA) proposed by Brage et al. (Supplementary Figure 1) (9). The hindfoot
60 deformity, reported as a risk factor for HV recurrence (20, 21), was assessed by
61 talonavicular coverage angle (TNCA), lateral talocalcaneal angle (LTCA), calcaneal
62 pitch angle (CPA), and talus-M1 angle (T1MTA) (22). To identify risk factors for HV
63 recurrence after background adjustment, we applied a generalized linear mixed model
64 (GLMM) to incorporate variations among surgeons and patients (15). The KURAMA

cohort study was approved by the Kyoto University Graduate School of Medicine Medical Ethics Committee (R0357), and informed consent was obtained from all patients. Programs and software used for statistical analyses were summarized in Supplementary Table 1.

In KURAMA cohort, we identified 45 feet in 33 RA patients who underwent DMO with a median follow-up of 50.2 months. DMO was performed by four surgeons (HI, MF, KM, and TF) during the study period. HV recurrence rate was 42.2% (Table 1). During the longitudinal observation of HVA, preoperative HVA was significantly higher in the non-recurrent group but corrected to similar levels after surgery (Supplementary Figure 2). However, the difference in HVA between recurrent and non-recurrent groups gradually became more prominent over time (Supplementary Figure 2). Interestingly, non-recurrent patients displayed no significant worsening of HVA postoperatively within the follow-up period (Supplementary Figure 2). The preoperative median age, body mass index (BMI), Clinical Disease Activity Index (CDAI), JSSF (the Japanese Society for Surgery of the Foot) RA foot and ankle scale (23), concomitant usage of methotrexate (MTX), glucocorticoids (GCs), and biological/targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs) were summarized in Table 1. Preoperative disease activity and medication usage did not significantly affect HV

83 recurrence (Table 1). Also, time-averaged disease activity (24), assessed by CDAI,
84 during the follow-up period did not differ between recurrent and non-recurrent groups
85 (Table 1). In the radiographic parameters, postoperative HV recurrence was associated
86 with greater preoperative HVA and 1TMTJA (Table 1 and Supplementary Figure 2).
87 The other radiographic parameters known as risk factors for postoperative HV
88 recurrence, such as inter-metatarsal angle, Hardy's classification, did not show
89 significant differences (Table 1) (25-27). There was no round sign positive (type R)
90 patient in both groups (28). None of the radiographic parameters of the hindfoot
91 assessed by TNCA, LTCA, CPA, and T1MTA were significantly correlated with HVA
92 preoperatively and at the last visit, consistent with the previous report (29)
93 (Supplementary Figure 3). We next performed GLMM to identify risk factors for HV
94 recurrence to account for inter-surgeon and inter-patient variations. Age, sex, BMI, dose
95 of MTX and PSL, use of b/tsDMARDs, preoperative HVA, preoperative inter-
96 metatarsal angle, postoperative inter-metatarsal angle, and 1TMTJA were used as
97 covariates (fixed effect) with patient- and surgeon-specific random intercepts. GLMM
98 revealed that 1TMTJA and preoperative HVA significantly positively correlated with
99 the HVA at the last visit (Figure 1). Receiver Operating Characteristic (ROC) curve
100 indicated that 1TMTJA had excellent predictive accuracy with Area Under the Curve

(AUC) of 0.90 (Supplementary Figure 4). Setting the threshold of 1TMTJA at 15° , 20 feet had $1\text{TMTJA} \geq 15^\circ$, and 25 feet had $1\text{TMTJA} < 15^\circ$. Among 20 feet with $1\text{TMTJA} \geq 15^\circ$, 16 feet (80.0%) showed HV recurrence, while HV recurrence was observed in 3 of 25 feet (12.0%) with $1\text{TMTJA} < 15^\circ$ (Supplementary Figure 5). Sensitivity, specificity, positive predictive value, and negative predictive value for HV recurrence were 84.21%, 84.62%, 80.0%, and 88.0%, respectively.

Although there is no consensus on the definition of postoperative HV recurrence, the reported rate of HV recurrence in RA was 4.5% -60 % (3, 19, 30). Kushioka et al. and Takakubo et al. separately reported the prevalence of HV recurrence in RA patients with the exact definition of recurrence as our study ($\text{HVA} \geq 20^\circ$) (3, 19). Kushioka et al. reported 16% recurrence in a mean follow-up of 35.3 months (19). Takakubo et al. reported different HV recurrence rates based on the type of the concomitant surgery for the lesser toe; they observed 32% recurrence when joint-preserving surgery was conducted for the lesser toes, while they reported 60% recurrence when resection arthroplasty was performed for the lesser toes (3). Of Note, their outcomes were based on modified Scarf osteotomy and modified Mann method, which have a higher potential for HV correction but may have higher invasiveness and complication rates compared to DMO (31). Our findings suggest that preoperative

measurement of 1TMTJA may make it possible to screen appropriate patients for DMO. RA disease activity can lead to progressive forefoot deformity, as reported by Shi et al. (32). Kushioka et al. reported the association between RA activity control and HV recurrence after HV correction (19). However, in our study, there was no statistical difference in preoperative and postoperative time-averaged CDAI (Table 1). Also, treatment did not correlate with HV recurrence in GLMM. Therefore, further studies are needed on the association between treatment, disease activity, and HV in RA.

In summary, this study demonstrates that the inclination of the medial cuneiform articular surface, measured by 1TMTJA, is an independent risk factor for post-DMO HV recurrence in RA patients. Notably, disease activity and medication did not impact recurrence, underscoring the importance of anatomical factors in surgical outcomes.

References

1. Smolen JS, Aletaha D, Barton A, Burmester GR, Emery P, Firestein GS, et al. Rheumatoid arthritis. Nat Rev Dis Primers. 2018;4:18001.
2. Fujii T, Nishi E, Ito H, Yoshitomi H, Furu M, Okabe N, et al. Nardilysin is involved in autoimmune arthritis via the regulation of tumour necrosis factor alpha secretion. RMD Open. 2017;3(1):e000436.

- 138 3. Takakubo Y, Wanezaki Y, Oki H, Naganuma Y, Shibuya J, Honma R, et al. Forefoot
139 Deformities in Patients with Rheumatoid Arthritis: Mid- to Long-Term Result of Joint-Preserving
140 Surgery in Comparison with Resection Arthroplasty. *Int J Environ Res Public Health*. 2021;18(21).
- 141 4. Coughlin MJ, Jones CP, Viladot R, Golano P, Grebing BR, Kennedy MJ, et al. Hallux
142 valgus and first ray mobility: a cadaveric study. *Foot Ankle Int*. 2004;25(8):537-44.
- 143 5. Smith BW, Coughlin MJ. The first metatarsocuneiform joint, hypermobility, and hallux
144 valgus: what does it all mean? *Foot Ankle Surg*. 2008;14(3):138-41.
- 145 6. Espinosa N, Wirth SH. Tarsometatarsal arthrodesis for management of unstable first ray
146 and failed bunion surgery. *Foot Ankle Clin*. 2011;16(1):21-34.
- 147 7. Popelka S, Hromadka R, Vavrik P, Bartak V, Popelka S, Jr., Sosna A. Hypermobility of
148 the first metatarsal bone in patients with rheumatoid arthritis treated by Lapidus procedure. *BMC*
149 *Musculoskelet Disord*. 2012;13:148.
- 150 8. Mann RA CM. Hallux valgus—etiology, anatomy, treatment and surgical considerations.
151 *Clin Orthop Relat Res*. 1981;157:31-41.
- 152 9. Brage ME, Holmes JR, Sangeorzan BJ. The influence of x-ray orientation on the first
153 metatarsocuneiform joint angle. *Foot Ankle Int*. 1994;15(9):495-7.
- 154 10. Fritz GR, Prieskorn D. First metatarsocuneiform motion: a radiographic and statistical
155 analysis. *Foot Ankle Int*. 1995;16(3):117-23.

156 11. Koury K, Staggars JR, Pinto MC, Godoy-Santos AL, Smyth NA, Shah AB, et al.
157 Radiographic Assessment of First Tarsometatarsal Joint Shape and Orientation. *Foot Ankle Int.*
158 2019;40(12):1438-46.

159 12. Yano K, Ikari K, Tobimatsu H, Tominaga A, Okazaki K. Joint-Preserving Surgery for
160 Forefoot Deformities in Patients with Rheumatoid Arthritis: A Literature Review. *Int J Environ*
161 *Res Public Health.* 2021;18(8).

162 13. Raikin SM, Miller AG, Daniel J. Recurrence of hallux valgus: a review. *Foot Ankle Clin.*
163 2014;19(2):259-74.

164 14. Watanabe K, Kubota M, Tanaka H, Nishiyama T, Hirao M, Fukushi JI, et al. Japanese
165 Orthopaedic Association (JOA) Clinical Practice Guidelines on the Management of Hallux Valgus
166 - Secondary publication. *J Orthop Sci.* 2024;29(1):1-26.

167 15. Fujii T, Murata K, Onizawa H, Onishi A, Tanaka M, Murakami K, et al. Management
168 and treatment outcomes of rheumatoid arthritis in the era of biologic and targeted synthetic
169 therapies: evaluation of 10-year data from the KURAMA cohort. *Arthritis Res Ther.* 2024;26(1):16.

170 16. Arnett FC, Edworthy SM, Bloch DA, McShane DJ, Fries JF, Cooper NS, et al. The
171 American Rheumatism Association 1987 revised criteria for the classification of rheumatoid
172 arthritis. *Arthritis Rheum.* 1988;31(3):315-24.

173 17. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO, 3rd, et al. 2010

174 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European
175 League Against Rheumatism collaborative initiative. *Arthritis Rheum.* 2010;62(9):2569-81.

176 18. Ishie S, Ito H, Azukizawa M, Furu M, Ishikawa M, Ogino H, et al. Delayed wound healing
177 after forefoot surgery in patients with rheumatoid arthritis. *Mod Rheumatol.* 2015;25(3):367-72.

178 19. Kushioka J, Hirao M, Tsuboi H, Ebina K, Noguchi T, Nampei A, et al. Modified Scarf
179 Osteotomy with Medial Capsule Interposition for Hallux Valgus in Rheumatoid Arthritis: A Study
180 of Cases Including Severe First Metatarsophalangeal Joint Destruction. *J Bone Joint Surg Am.*
181 2018;100(9):765-76.

182 20. Hirao M, Ebina K, Tsuboi H, Noguchi T, Hashimoto J, Yoshikawa H. Appearance of
183 hindfoot valgus deformity and recurrence of hallux valgus in the very early period after hallux
184 valgus surgery in a poorly controlled rheumatoid arthritis case: A case report. *Mod Rheumatol.*
185 2019;29(2):367-9.

186 21. Gines-Cespedosa A, Perez-Prieto D, Muneton D, Gonzalez-Lucena G, Millan A, de
187 Zabala S, et al. Influence of Hindfoot Malalignment on Hallux Valgus Operative Outcomes. *Foot*
188 *Ankle Int.* 2016;37(8):842-7.

189 22. Bourdet C, Seringe R, Adamsbaum C, Glorion C, Wicart P. Flatfoot in children and
190 adolescents. Analysis of imaging findings and therapeutic implications. *Orthop Traumatol Surg*
191 *Res.* 2013;99(1):80-7.

192 23. Niki H, Aoki H, Inokuchi S, Ozeki S, Kinoshita M, Kura H, et al. Development and
193 reliability of a standard rating system for outcome measurement of foot and ankle disorders I:
194 development of standard rating system. *J Orthop Sci.* 2005;10(5):457-65.

195 24. Tsuji H, Yano K, Furu M, Yamakawa N, Ikari K, Hashimoto M, et al. Time-averaged
196 disease activity fits better joint destruction in rheumatoid arthritis. *Sci Rep.* 2017;7(1):5856.

197 25. Ezzatvar Y, Lopez-Bueno L, Fuentes-Aparicio L, Duenas L. Prevalence and
198 Predisposing Factors for Recurrence after Hallux Valgus Surgery: A Systematic Review and Meta-
199 Analysis. *J Clin Med.* 2021;10(24).

200 26. Deenik AR, de Visser E, Louwerens JW, de Waal Malefijt M, Draijer FF, de Bie RA.
201 Hallux valgus angle as main predictor for correction of hallux valgus. *BMC Musculoskelet Disord.*
202 2008;9:70.

203 27. Hardy RH, Clapham JC. Observations on hallux valgus; based on a controlled series. *J*
204 *Bone Joint Surg Br.* 1951;33-B(3):376-91.

205 28. Okuda R, Kinoshita M, Yasuda T, Jotoku T, Kitano N, Shima H. The shape of the lateral
206 edge of the first metatarsal head as a risk factor for recurrence of hallux valgus. *J Bone Joint Surg*
207 *Am.* 2007;89(10):2163-72.

208 29. Yano K, Ikari K, Nakayama M, Sakuma Y, Imamura H, Tobimatsu H, et al. The impact
209 of hindfoot deformities for the recurrence of hallux valgus after joint-preserving surgeries for

210 rheumatoid forefoot deformities. *Foot Ankle Surg.* 2019;25(3):348-53.

211 30. Bhavikatti M, Sewell MD, Al-Hadithy N, Awan S, Bawarish MA. Joint preserving surgery

212 for rheumatoid forefoot deformities improves pain and corrects deformity at midterm follow-up.

213 *Foot (Edinb).* 2012;22(2):81-4.

214 31. Lee KB, Cho NY, Park HW, Seon JK, Lee SH. A comparison of proximal and distal

215 Chevron osteotomy, both with lateral soft-tissue release, for moderate to severe hallux valgus in

216 patients undergoing simultaneous bilateral correction: a prospective randomised controlled trial.

217 *Bone Joint J.* 2015;97-B(2):202-7.

218 32. Shi K, Hayashida K, Tomita T, Tanabe M, Ochi T. Surgical treatment of hallux valgus

219 deformity in rheumatoid arthritis: clinical and radiographic evaluation of modified Lapidus

220 technique. *J Foot Ankle Surg.* 2000;39(6):376-82.

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Figure legends

Figure 1. Correlation between 1TMTJA, preoperative HVA, and HVA at the last observation.

A scatter plot showing correlation between 1TMTJA, preoperative HVA and HVA at the last observation. A line in the plots represents a regression line computed with generalized linear mixed model.

Author contributions:

TF conceptualized and designed this study. HI, MF, KoiM, and TF performed surgery. TF, KoiM, KosM, HO, AO, HI, MF and MT acquired data. TF performed data analysis, and TF and KoiM performed data interpretation. TF prepared the manuscript. AM and SM supervised the study and approved the manuscript submission. All authors discussed the results and contributed to the final manuscript.

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253 Table 1: Baseline characteristics

	All (n=45)	Non-recurrent (n=26)	Recurrent (n=19)	p-value
Age, median (IQR), yr	67 (14)	67 (6.5)	62.0 (17.5)	0.354
Sex, female %	86.70%	92.30%	78.90%	0.391
BMI, median (IQR), kg/m ²	22.1 (6.71)	22.3 (5.97)	22.0 (7.19)	0.416
MTX, median (IQR), mg	4.0 (6.0)	6.0 (4.0)	0 (6.0)	0.054
MTX use, %	64.4%	76.9%	47.4%	0.084
GC, median (IQR), mg	0.5 (3.0)	0 (3.38)	1.5 (3.0)	0.768
GC use, %	53.3%	46.20%	63.20%	0.408
b/tsDMARDs use,%	42.2%	36.5%	47.4%	0.77
Preoperative CDAI, median (IQR)	7.45 (8.98)	8.0 (8.4)	4.0 (5.5)	0.367
Postoperative Time-averaged CDAI, median (IQR)	9.15 (4.20)	9.3 (2.01)	7.24 (4.24)	0.223
Preoperative JSSF scale, median (IQR)	56 (17.0)	56 (16.5)	56.5 (18.5)	0.296
Preoperative HVA, median (IQR), °	47.6 (16.5)	42.4 (10.3)	51.8 (19.6)	0.041
Preoperative IMA, median (IQR), °	16.0 (6.1)	16.7 (5.0)	15.0 (4.70)	0.528
Preoperative Hardy, median (IQR)	7.0 (1.0)	7.0 (1.0)	7.0 (1.0)	0.289
Postoperative IMA, median (IQR), °	4.3 (3.5)	4.25 (3.32)	4.4 (3.9)	0.915
1TMTJA, median (IQR), °	11.4 (12.3)	8.6 (4.35)	20.4 (3.80)	p<0.001
Surgery for lesser toes, %	84.40%	84.60%	84.20%	1

IQR: Interquartile range, BMI: Body mass index, MTX: Methotrexate, GC: Glucocorticoid (prednisolone equivalent), b/tsDMARDs: biological/targeted synthetic disease-modifying antirheumatic drugs, CDAI: Clinical disease activity index, JSSF: Japanese Society for Surgery of the Foot. Statistics used; Welch's t test or Wilcoxon rank sum test for continuous variables and chi-square test with Yate's correction for categorical variables.

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