

Influences of advanced age in rheumatoid arthritis: A multicentre ultrasonography cohort study

関節リウマチにおける高齢化の影響：多施設超音波コホート研究

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目的：

本研究では、生物学的製剤または JAK 阻害薬 (b/tsDMARD) 未投与の関節リウマチ (RA) 患者において、年齢が臨床的特徴および治療転帰に及ぼす影響を評価することを目的としました。

方法：

多施設超音波前向き観察コホート (KUDOS) において、b/tsDMARD 治療を導入した b/tsDMARD ナイーブ RA 患者 234 例を対象に解析しました。ベースライン時の臨床的特徴および 12 ヶ月後の転帰を 60 歳以上群と 60 歳未満群で比較しました。

結果：

60 歳未満群 (n=78) と比較して、60 歳以上群 (n=156) ではベースライン時の炎症マーカー値と超音波複合スコア、特に手関節のスコアが高値を示しました (Table 1)。年齢はベースライン時の超音波検査スコアと有意な正の相関を示した (Figure 1) が、重回帰分析では年齢は有意な独立変数とはなりませんでした。60 歳以上群では、作用機序 (MOA) の異なる治療薬による転帰に差はみられず、重回帰分析により、MOA は 12 ヶ月後の臨床疾患活動性指数に有意な影響を与えないことが示されました。

結論：

高齢 RA 患者は、特徴的な臨床像が認められたものの、治療薬 MOA は臨床的転帰および超音波評価結果と有意な関連を示しませんでした。

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Table 3. MOAにより層別化した60歳以上のRA患者における患者の特徴と転帰の比較

	TNF inhibitor, <i>n</i> = 54	IL-6 inhibitor, <i>n</i> = 24	CTLA-4Ig, <i>n</i> = 64	JAK inhibitor, <i>n</i> = 14	<i>P</i> -value ^a
At the time of recruitment:					
Age, yrs	70.0 [65.0, 76.0]	71.0 [65.0, 74.8]	75.0 [70.0, 79.2]	72.0 [65.2, 77.8]	0.005
Male, <i>n</i> (%)	16 (29.6)	4 (16.7)	15 (23.4)	3 (21.4)	0.64
Disease duration, months	20.5 [7.2, 93.8]	72.0 [17.0, 102.0]	24.5 [10.8, 120.0]	81.0 [15.2, 150.5]	0.26
Smoking history, <i>n</i> (%)	15 (28.3)	6 (27.3)	12 (20.0)	5 (35.7)	0.58
RF-positive, <i>n</i> (%)	36 (70.6)	15 (68.2)	47 (75.8)	12 (85.7)	0.62
ACPA-positive, <i>n</i> (%)	41 (78.8)	20 (87.0)	52 (83.9)	11 (78.6)	0.80
ILD, <i>n</i> (%)	7 (13.5)	8 (38.1)	19 (30.2)	4 (28.6)	0.088
MTX use, <i>n</i> (%)	33 (62.3)	6 (26.1)	24 (38.1)	8 (57.1)	0.009
MTX dose, mg/week (0 mg for no use)	8.0 [0.0, 10.0]	0.0 [0.0, 1.0]	0.0 [0.0, 8.0]	5.0 [0.0, 9.5]	0.006
PSL use, <i>n</i> (%)	30 (55.6)	8 (33.3)	34 (53.1)	7 (50.0)	0.31
PSL dose, mg/day (0 mg for no use)	2.0 [0.0, 5.0]	0.0 [0.0, 3.5]	1.0 [0.0, 5.0]	0.5 [0.0, 2.5]	0.25
Use of csDMARDs other than MTX, <i>n</i> (%)	13 (24.1)	8 (33.3)	31 (48.4)	4 (28.6)	0.045
TJC, <i>n</i>	4.0 [2.0, 7.0]	4.0 [2.0, 9.5]	4.5 [2.0, 9.0]	5.0 [2.2, 6.8]	0.87
SJC, <i>n</i>	5.0 [3.0, 7.0]	4.0 [2.5, 6.0]	6.0 [2.0, 9.0]	2.0 [1.0, 4.8]	0.17
Patient global VAS, mm	33.0 [21.2, 53.8]	39.5 [20.0, 64.2]	46.5 [26.5, 65.0]	41.5 [30.0, 50.0]	0.34
Patient pain VAS, mm	34.0 [20.0, 50.8]	25.0 [15.0, 65.0]	41.0 [30.0, 70.0]	40.0 [26.8, 75.0]	0.24
Physician global VAS, mm	36.5 [25.0, 50.0]	40.5 [20.0, 51.5]	40.0 [30.0, 60.0]	42.5 [26.2, 52.2]	0.36
ESR, mm/h	35.0 [25.0, 64.2]	43.0 [33.0, 65.0]	41.5 [26.0, 64.0]	37.0 [21.5, 53.0]	0.69
CRP, mg/dL	0.8 [0.2, 1.9]	1.2 [0.7, 3.5]	0.9 [0.4, 3.4]	2.0 [0.8, 2.2]	0.22
DAS28 (ESR)	4.7 [4.1, 5.5]	5.2 [4.0, 5.9]	5.1 [4.3, 5.7]	4.6 [3.8, 5.8]	0.58
DAS28 (CRP)	4.2 [3.4, 4.6]	4.1 [3.5, 5.1]	4.2 [3.5, 5.3]	3.8 [3.6, 5.1]	0.56
SDAI	18.8 [13.9, 25.9]	20.3 [12.0, 28.5]	21.0 [14.4, 30.7]	14.8 [13.3, 27.3]	0.41
CDAI	17.2 [13.0, 23.9]	18.9 [9.8, 25.8]	18.9 [13.8, 28.9]	13.2 [11.3, 22.6]	0.41
Total GS score	11.0 [6.0, 18.0]	11.0 [5.8, 19.5]	12.0 [7.0, 22.0]	9.5 [6.5, 21.5]	0.84
Total PD score	5.5 [3.2, 12.0]	7.0 [3.0, 14.5]	6.0 [3.0, 14.5]	5.5 [3.0, 12.2]	0.98
Total combined score	11.5 [6.0, 22.5]	11.5 [6.0, 19.5]	12.0 [7.0, 22.5]	9.5 [6.8, 22.5]	0.94
At 12 months:					
DAS28 (ESR)	2.6 [1.9, 3.9]	2.4 [1.4, 3.4]	2.8 [2.2, 3.8]	2.5 [2.2, 2.8]	0.22
DAS28 (CRP)	2.0 [1.5, 2.9]	2.1 [1.3, 2.5]	2.0 [1.5, 3.0]	1.5 [1.4, 1.7]	0.30
SDAI	5.1 [1.2, 9.5]	4.9 [1.4, 8.0]	3.8 [1.1, 11.2]	3.1 [2.0, 5.8]	0.82
CDAI	5.0 [1.0, 8.6]	4.5 [1.3, 7.2]	3.2 [0.8, 11.0]	3.0 [2.0, 5.6]	0.88
Total GS score	5.0 [2.0, 9.0]	3.5 [2.0, 8.2]	6.5 [3.2, 12.8]	5.5 [2.2, 7.8]	0.16
Total PD score	1.0 [0.0, 4.0]	0.0 [0.0, 3.0]	1.0 [0.0, 4.5]	0.0 [0.0, 1.8]	0.37
Total combined score	4.5 [1.0, 9.8]	3.5 [2.0, 8.2]	6.0 [3.0, 12.5]	5.5 [2.2, 7.8]	0.20
DAS28 (ESR) remission	25 (46.3)	14 (58.3)	27 (42.2)	7 (53.8)	0.56
DAS28 (CRP) remission	32 (59.3)	14 (58.3)	36 (56.2)	11 (78.6)	0.49
SDAI remission	24 (44.4)	9 (37.5)	29 (45.3)	8 (57.1)	0.71
CDAI remission	22 (40.7)	9 (37.5)	30 (46.9)	5 (35.7)	0.78
US Doppler remission	24 (46.2)	12 (52.2)	25 (39.7)	8 (57.1)	0.56
US strict remission	6 (11.1)	3 (12.5)	4 (6.3)	0 (0.0)	0.45
US semi-strict remission	9 (16.7)	6 (25.0)	10 (15.9)	3 (21.4)	0.76

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Table 1. 60歳以上と60歳未満のRA患者の特徴の比較

	Overall, <i>n</i> = 234	Patients <60 y.o., <i>n</i> = 78	Patients ≥60 y.o., <i>n</i> = 156	<i>P</i> -value
At the time of recruitment:				
Age, yrs	66.0 [56.0, 75.0]	50.0 [42.2, 56.0]	72.0 [66.0, 78.0]	<0.001
Male, <i>n</i> (%)	54 (23.1)	16 (20.5)	38 (24.4)	0.62
Disease duration, months	24.0 [9.0, 96.0]	15.0 [9.0, 76.5]	26.0 [10.5, 120.0]	0.029
Smoking history, <i>n</i> (%)	58 (26.1)	20 (27.4)	38 (25.5)	0.89
RF-positive, <i>n</i> (%)	162 (71.4)	52 (66.7)	110 (73.8)	0.33
ACPA-positive, <i>n</i> (%)	184 (80.3)	60 (76.9)	124 (82.1)	0.45
ILD, <i>n</i> (%)	44 (19.7)	6 (8.2)	38 (25.3)	0.005
MTX use, <i>n</i> (%)	126 (55.3)	55 (73.3)	71 (46.4)	<0.001
MTX dose, mg/week	6.0 [0.0, 10.0]	8.0 [0.0, 10.0]	0.0 [0.0, 8.0]	<0.001
Use of csDMARDs other than MTX, <i>n</i> (%)	69 (29.5)	13 (16.7)	56 (35.9)	0.004
PSL use, <i>n</i> (%)	115 (49.1)	36 (46.2)	79 (50.6)	0.61
PSL dose, mg/day	0.0 [0.0, 5.0]	0.0 [0.0, 5.0]	1.0 [0.0, 5.0]	0.58
TJC, <i>n</i>	4.0 [2.0, 9.0]	4.5 [2.0, 10.0]	4.0 [2.0, 8.0]	0.67
SJC, <i>n</i>	4.0 [2.0, 8.0]	4.0 [2.0, 7.0]	5.0 [2.0, 8.0]	0.26
Patient global VAS, mm	43.5 [25.0, 65.0]	50.0 [25.0, 72.2]	40.0 [25.0, 64.0]	0.131
Patient pain VAS, mm	40.0 [25.0, 66.5]	50.0 [30.0, 68.0]	40.0 [22.0, 65.0]	0.40
Physician global VAS, mm	40.0 [25.0, 60.0]	49.5 [25.0, 60.0]	40.0 [25.0, 53.5]	0.30
ESR, mm/h	38.0 [22.0, 62.0]	35.5 [15.2, 55.5]	41.0 [26.0, 64.0]	0.034
CRP, mg/dL	0.9 [0.3, 2.3]	0.6 [0.1, 1.9]	1.2 [0.4, 2.7]	0.016
DAS28 (ESR)	4.9 [4.1, 5.7]	4.9 [4.0, 5.8]	4.9 [4.1, 5.6]	0.69
DAS28 (CRP)	4.1 [3.5, 5.1]	4.0 [3.4, 5.1]	4.1 [3.5, 5.0]	0.74
SDAI	20.2 [13.6, 29.3]	20.4 [14.1, 30.4]	19.8 [13.5, 29.1]	0.80
CDAI	18.5 [13.0, 26.4]	20.0 [14.0, 26.2]	18.0 [12.9, 26.2]	0.51
Total GS score	11.0 [6.0, 19.0]	9.0 [5.0, 14.0]	11.0 [6.0, 21.5]	0.052
Total PD score	6.0 [3.0, 12.0]	5.0 [1.0, 10.0]	6.0 [3.0, 13.0]	0.086
Total combined score	11.0 [6.0, 19.2]	9.0 [6.0, 14.0]	12.0 [6.0, 23.0]	0.049
Sum of GS score of PIP	2.0 [0.0, 5.0]	2.0 [0.0, 4.0]	2.0 [0.0, 6.0]	0.26
Sum of GS score of MCP	4.0 [2.0, 10.0]	4.0 [1.0, 9.0]	5.0 [2.0, 11.0]	0.27
Sum of GS score of wrists	3.0 [2.0, 4.0]	2.0 [1.0, 4.0]	3.0 [2.0, 4.0]	0.014
Sum of PD score of PIP	0.0 [0.0, 3.0]	0.0 [0.0, 2.8]	0.0 [0.0, 3.0]	0.25
Sum of PD score of MCP	2.0 [0.0, 6.0]	1.0 [0.0, 5.8]	2.0 [0.0, 7.0]	0.067
Sum of PD score of wrists	2.0 [1.0, 4.0]	2.0 [0.0, 4.0]	2.0 [1.0, 4.0]	0.082
Sum of CS score of PIP	2.0 [0.0, 5.0]	2.0 [0.0, 4.0]	2.0 [0.0, 6.0]	0.25
Sum of CS score of MCP	4.0 [2.0, 11.0]	4.0 [1.0, 9.0]	5.0 [2.0, 11.0]	0.21
Sum of CS score of wrists	3.0 [2.0, 4.0]	2.5 [1.0, 4.0]	4.0 [2.0, 4.0]	0.012
MOA used:				<0.0001
TNF inhibitor, <i>n</i> (%)	94 (40.2)	40 (51.3)	54 (34.6)	
IL-6 inhibitor, <i>n</i> (%)	49 (20.9)	25 (32.1)	24 (15.4)	
CTLA4-Ig, <i>n</i> (%)	75 (32.1)	11 (14.1)	64 (41.0)	
JAK inhibitor, <i>n</i> (%)	16 (6.8)	2 (2.6)	14 (9.0)	
At 12 months:				
DAS28 (ESR)	2.6 [1.8, 3.8]	2.5 [1.7, 4.0]	2.7 [2.0, 3.7]	0.95
DAS28 (CRP)	2.0 [1.4, 2.9]	2.2 [1.4, 3.1]	2.0 [1.4, 2.8]	0.38
SDAI	4.8 [1.3, 9.6]	6.9 [1.6, 11.7]	3.8 [1.3, 8.6]	0.116
CDAI	4.5 [1.2, 9.0]	6.4 [1.5, 10.7]	3.5 [1.0, 8.1]	0.059
Total GS score	5.0 [2.0, 10.0]	4.0 [2.0, 9.0]	5.0 [2.0, 10.0]	0.24
Total PD score	1.0 [0.0, 3.0]	0.0 [0.0, 3.0]	1.0 [0.0, 3.0]	0.26
Total combined score	5.0 [2.0, 10.2]	4.0 [2.0, 10.0]	5.0 [2.0, 11.0]	0.23
DAS28 (ESR) remission	113 (49.1)	40 (53.3)	73 (47.1)	0.46
DAS28 (CRP) remission	133 (57.1)	40 (51.9)	93 (59.6)	0.33
SDAI remission	97 (41.6)	27 (35.1)	70 (44.9)	0.60
CDAI remission	92 (39.5)	26 (33.8)	66 (42.3)	0.27
US Doppler remission	110 (48.5)	41 (54.7)	69 (45.4)	0.24
US strict remission	24 (10.4)	11 (14.7)	13 (8.4)	0.22
US semi-strict remission	48 (20.9)	20 (26.7)	28 (18.1)	0.18

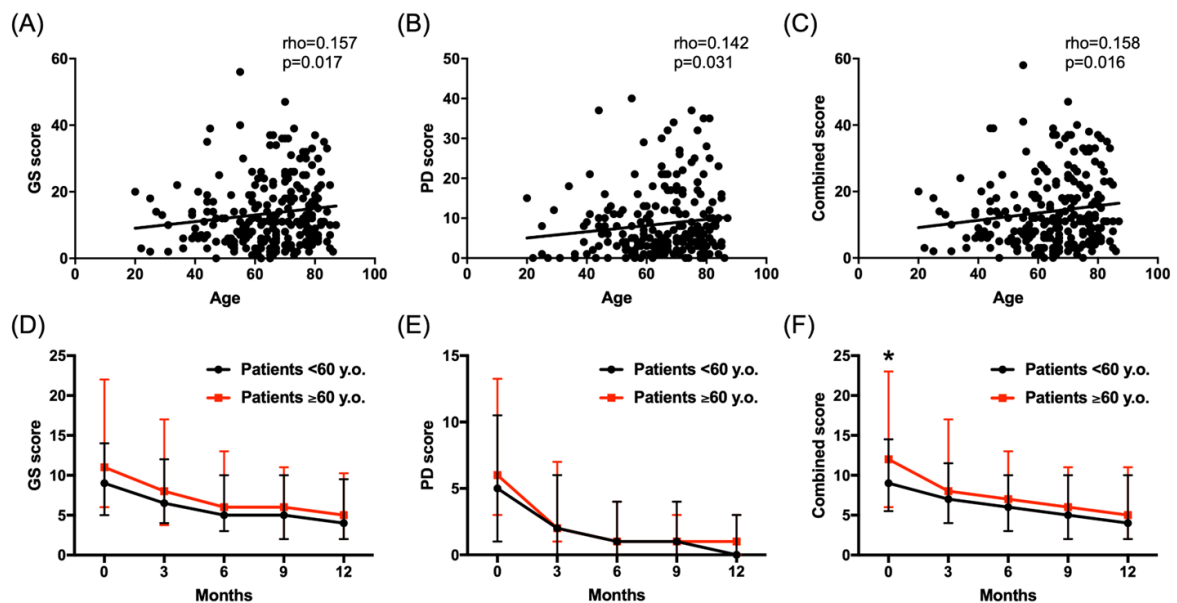
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Table 2. ベースライン時の超音波複合スコアと12ヵ月後のCDAIに関する重回帰分析

Characteristic	Coefficient (95% CI)	P-value
Ultrasound combined score at baseline		
(Intercept)	1.003 (-6.827-8.834)	0.80
Age	0.085 (-0.016-0.185)	0.097
Male	-4.025 (-7.557 to -0.494)	0.026
Disease duration (months)	0.011 (-0.001-0.023)	0.074
Smoking	0.604 (-2.717-3.925)	0.72
RF	1.158 (-2.143-4.458)	0.49
ACPA	-2.797 (-6.582-0.988)	0.15
ILD	-1.632 (-5.394-2.129)	0.39
MTX use	-0.556 (-4.219-3.107)	0.77
Use of csDMARDs other than MTX	0.315 (-3.637-4.267)	0.88
PSL use	0.036 (-2.647-2.719)	0.98
ESR at baseline	0.004 (-0.055-0.062)	0.90
CRP at baseline	0.850 (0.123-1.578)	0.022
CDAI at baseline	0.385 (0.274-0.495)	<0.001
CDAI at 12 months		
(Intercept)	13.615 (-2.215-29.445)	0.091
Age	-0.129 (-0.345-0.087)	0.24
Male	-0.819 (-4.419-2.781)	0.65
Disease duration (months)	-0.006 (-0.016-0.004)	0.21
Smoking	-0.627 (-4.138-2.883)	0.72
RF	-1.718 (-5.204-1.768)	0.33
ACPA	0.701 (-3.503-4.905)	0.74
ILD	5.557 (2.136-8.978)	0.002
MTX use	-0.34 (-4.034-3.354)	0.86
Use of csDMARDs other than MTX	-1.26 (-5.004-2.485)	0.51
PSL use	-2.118 (-4.856-0.62)	0.13
ESR at baseline	0.012 (-0.045-0.069)	0.68
CRP at baseline	0.22 (-0.467-0.907)	0.53
CDAI at baseline	0.181 (0.072-0.291)	0.001
MOA		
TNF inhibitor		
IL-6 inhibitor ^a	-3.081 (-7.394-1.232)	0.16
CTLA4-Ig ^a	-0.014 (-3.161-3.133)	0.99
JAK inhibitor ^a	-2.890 (-7.549-1.769)	0.22

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Figure 1. ベースラインにおける年齢と総GSスコア(a)、総PDスコア(b)、および総複合スコア(c)との相関 (rho: スピアマンの相関係数)



Kawahara C, Fukui S, et al. Mod Rheumatol. 2024;34(6):1142-1148, Figure 1