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Impact of age at disease onset on clinical manifestations and prognosis in systemic lupus erythematosus

Sistemik lupus eritematozusta hastalık başlangıç yaşının klinik belirtiler ve prognoz üzerindeki etkisi

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Abstract

Objective: To assess age-related differences in demographic, clinical, and treatment characteristics of systemic lupus erythematosus (SLE) patients and evaluate outcomes based on age at disease onset.

Methods: Patients diagnosed with SLE who met 2012 Systemic Lupus International Collaborating Clinics (SLICC) criteria were retrospectively evaluated. Patients were classified based on age at onset: adult-onset (18-49 years) and late-onset (≥50 years). Demographic, clinical, laboratory characteristics and outcomes of adult and late-onset groups were compared. Disease damage was evaluated with the SLICC/American College of Rheumatology damage index (SDI). To assess the effect of age on mortality, Cox regression analysis was performed with the selected variables that were causally associated with the outcome.

Results: Among 519 patients, 88.1% were female, with a mean diagnosis age of 36.6 years. Adult-onset SLE represented 82.3% of cases, while 17.7% had late-onset disease. Neurological involvement was more frequent in adult-onset SLE (25.8% *vs.* 16.3%), as was renal involvement (41.1% *vs.* 26.1%). Anti-ribonucleoprotein antibodies were more prevalent in adult-onset SLE (24.7% *vs.* 7.1%, p<0.001). Damage accrual was observed in 40.3% of patients, without significant differences in SDI scores between groups. After a median follow-up of 9.2 years, 10.8% of patients died, with a higher mortality rate in late-onset SLE (20.7% *vs.* 8.7%, p=0.001). Cox regression showed age at SLE onset was independently associated with increased mortality (hazard ratio: 1.09, 95% confidence interval: 1.06-1.11, p<0.001).

Conclusion: Age at SLE onset is associated with distinct clinical features and outcomes. Late-onset SLE patients experience higher mortality, emphasizing the need for age-specific approaches in SLE management.

Keywords: Systemic lupus eryhthematosus, age at onset, damage, mortality

Özet

Amaç: Bu çalışmanın amacı, sistemik lupus eritematozus (SLE) hastalarında yaşa bağlı demografik, klinik ve tedavi özelliklerindeki farklılıkları değerlendirmek ve hastalık başlangıç yaşına göre prognozu incelemektir.

Yöntem: 2012 Sistemik Lupus Uluslararası İşbirliği Klinikleri (SLICC) kriterlerini karşılayan SLE tanılı hastalar retrospektif olarak değerlendirildi. Hastalar, hastalık başlangıç yaşlarına göre yetişkin başlangıçlı (18-49 yaş) ve geç başlangıçlı (≥50 yaş) olmak üzere sınıflandırıldı. Yetişkin ve geç başlangıçlı grupların demografik, klinik, laboratuvar özellikleri ve sonuçları karşılaştırıldı. Hastalığa bağlı hasar, SLICC/Amerikan Romatoloji Koleji hasar indeksi (SDI) ile değerlendirildi. Yaşın mortalite üzerindeki etkisini incelemek için, sonuçla nedensel ilişkili değişkenlerin dahil edildiği Cox regresyon analizi uygulandı.

Bulgular: Toplam 519 hastanın %88,1'i kadın olup, ortalama tanı yaşı 36,6 yıl olarak belirlendi. Hastaların %82,3'ü yetişkin başlangıçlı, %17,7'si ise geç başlangıçlı SLE grubundaydı. Nörolojik tutulum yetişkin başlangıçlı SLE'de daha sık görüldü (%25,8'e karşı %16,3), aynı şekilde renal tutulum da daha yüksekti (%41,1'e karşı %26,1). Anti-ribonükleoprotein antikorları yetişkin başlangıçlı grupta daha yaygındı (%24,7'ye karşı %7,1, p<0,001). Hasar birikimi %40,3 hastada gözlenmiş olup, gruplar arasında SDI skorlarında anlamlı bir fark bulunmadı. Ortalama 9,2 yıllık takip süresi sonunda, hastaların %10,8'i hayatını kaybetti ve geç başlangıçlı SLE grubunda mortalite oranı daha yüksekti (%20,7'ye karşı %8,7, p=0,001). Cox regresyon analizi, SLE başlangıç yaşının bağımsız olarak artmış mortalite ile ilişkili olduğunu gösterdi (risk oranı: 1,09, %95 güven aralığı: 1,06-1,11, p<0,001).

Sonuç: Bu çalışmada, SLE başlangıç yaşı, klinik özellikler ve prognoz üzerinde farklılıklarla ilişkili olarak bulunmuştur. Geç başlangıçlı SLE hastalarında yüksek mortalite gözlenmiş olup, bu sonuç yaşa özgü yaklaşımların gerekliliğini vurgulamaktadır.

Anahtar Kelimeler: Sistemik lupus eritematozus, hastalık başlangıç yaşı, hasar, mortalite

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Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by a broad spectrum of clinical manifestations that can affect multiple organ systems.[1] The disease onset can vary significantly, occurring in individuals ranging from childhood to older adulthood. Understanding how the age at onset influences disease outcomes is crucial for optimizing management strategies and improving patient prognosis. Prior studies suggest that early-onset SLE, particularly in pediatric cases, often presents more aggressively, with higher rates of organ damage and complications, whereas late-onset SLE may exhibit distinct clinical features and outcomes.[2-7] Therefore, in this single-centre retrospective study, our objective was to assess the association between the age at SLE onset and key outcomes, including disease manifestations, cumulative damage, and survival.

Materials and Methods

In this study, we scrutinized the medical records of 579 patients who met the 2012 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria for SLE[8] and were evaluated in the adult rheumatology clinic between January 2010 and August 2021. Demographic, clinical, and treatment characteristics of all patients were retrospectively assessed, with clinical and treatment features recorded cumulatively. In contrast, for laboratory characteristics, the values at the initial evaluation or the first recorded values in our hospital data system were considered. Neurological involvement was determined based on the 1999 American College of Rheumatology (ACR) nomenclature and case definition for neuropsychiatric SLE.[9]

Patients were grouped into three different categories according to the age at onset of the disease: Childhood-onset (<18 years of age), adult-onset (18-49 years), and late-onset (≥50 years) SLE. To avoid selection bias, 60 (10.4%) patients with childhood-onset SLE were excluded from the study.

The SLICC/ACR damage index (SDI) is a widely used tool to evaluate the damage to organs in patients with SLE and captures damage resulting from both the disease process and its treatments. The SDI provides a cumulative score that reflects the extent of permanent damage.[10] It includes a variety of domains (41 items across 12 organ systems), including the renal, neuropsychiatric, cardiovascular, neurological, and musculoskeletal systems. In this study, the SDI was used to assess the long-term impact of the disease. To calculate SDI scores, only patients with a minimum follow-up period of 6 months were included, ensuring an accurate and reliable evaluation of disease progression. Follow-up time was defined as the duration from disease diagnosis to the last follow-up date or death.

We obtained approval from the Ethics Committee of Ankara University (approval number: İ9-592-21, date: 21.10.2021) and conducted the study in accordance with the Declaration of Helsinki.

Statistical Analysis

Categorical variables are presented as frequencies and percentages. In univariate of categorical variables, levels of significance were determined by means of the chi-square test or Fisher's exact probability test using contingency tables. Quantitative variables are shown as either median and 25th and 75th percentile (Q1-Q3) or as mean and standard deviation (SD). The Independent Samples t-test, or the Mann-Whitney U test as a non-parametric substitute, was used to analyse quantitative variables.

To demonstrate the association of age with overall mortality, Cox regression analyses were performed. The follow-up duration was determined as the gap-time from the diagnosis of SLE to the last visit for the survived patients and to death for the deceased patients. Based on the causal assumptions, adjustment for sex, SDI scores and immunosuppresant use was performed. A 95% confidence interval of corresponding hazard ratios (HR) which did not include a null effect was accepted as significant. Analyses were performed by using the SPSS software version 26.

Results

Characteristics of the Study Subjects

Of the 519 patients, 457 (88.1%) were female, and the mean age at SLE diagnosis was 36.6±13.4 years (31.7±8.7 and 58.9±7.4 for the adult-onset and the late-onset groups, respectively). The most common involvement was acute cutaneous lupus (57.0%), followed by hematological involvement (53.8%), synovitis (48.6%), renal involvement (38.9%), and neurological involvement (24.3%). Demographic and disease-related characteristics are shown in detail in Table 1.

The patients with adult-onset SLE comprised of 82.3% of the study cohort whereas it was 17.7% for the late-onset group. In terms of clinical phenotypes, renal and neurological involvements differed between two groups being both involvements more common in the adult-onset group. The proportions of patients with acute cutaneous lupus were similar, however, malar rash was more prevalent in the adult-onset SLE (37.2% *vs.* 26.1%, p=0.042).

Table 1. Demographic and clinical characteristics of the study population

	All cohort (n=519)	Adult-onset (n=427)	Late-onset (n=92)	p
Sex				0.726
Female, n (%)	457 (88.1)	375 (87.8)	82 (89.1)	
Male, n (%)	62 (11.9)	52 (12.2)	10 (10.9)	
Age at diagnosis, y, mean (SD)	36.6 (13.4)	31.7 (8.7)	58.9 (7.4)	<0.001
Fever, n (%)	69 (13.3)	56 (13.1)	13 (14.1)	0.795
Acute cutaneous lupus, n (%)	296 (57.0)	248 (58.1)	48 (52.2)	0.299
Photosensitivity	234 (45.1)	198 (46.4)	36 (39.1)	0.206
Malar rash	183 (35.3)	159 (37.2)	24 (26.1)	0.042
Others	17 (3.3)	14 (3.3)	3 (3.3)	1.00
Chronic cutaneous lupus, n (%)	59 (11.4)	49 (11.5)	10 (10.9)	0.868
DLE	57 (11.0)	47 (11.0)	10 (10.9)	0.969
Alopecia, n (%)	107 (20.6)	92 (21.5)	15 (16.3)	0.260
Oral or nasal ulcer, n (%)	120 (23.1)	102 (23.9)	18 (19.6)	0.372
Oral ulcer	117 (22.5)	100 (23.4)	17 (18.5)	0.304
Nasal ulcer	8 (1.5)	7 (1.6)	1 (1.1)	1.00
Synovitis, n (%)	252 (48.6)	208 (48.7)	44 (47.8)	0.877
Serositis, n (%)	92 (17.7)	76 (17.8)	16 (17.4)	0.926
Pleuritis	64 (12.3)	52 (12.2)	12 (13.0)	0.819
Pericarditis	51 (9.8)	41 (9.6)	10 (10.9)	0.711
Peritonitis	7 (1.3)	5 (1.2)	2 (2.2)	0.360
Renal involvement, n (%)	202 (38.9)	177 (41.5)	25 (27.2)	0.011
Nephrotic proteinuria	64 (12.3)	57 (13.3)	7 (7.6)	0.129
Neurological involvement, n (%)	126 (24.3)	112 (26.2)	14 (15.2)	0.025
Haematological involvement, n (%)	279 (53.8)	228 (53.4)	51 (55.4)	0.722
AIHA	94 (18.1)	78 (18.3)	16 (17.4)	0.843
Thrombocytopenia	120 (23.1)	101 (23.7)	19 (20.7)	0.536
Secondary APS, n (%)	66 (12.7)	53 (12.4)	13 (14.1)	0.654
Gestational	33 (6.4)	26 (6.1)	7 (7.6)	0.588
Vascular thrombosis	51 (9.8)	41 (9.6)	10 (10.9)	0.711
Lympadenopathy, n (%)	53 (10.2)	46 (10.8)	7 (7.6)	0.363
Livedo reticularis, n (%)	14 (2.7)	13 (3.0)	1 (1.1)	0.482
Raynaud phenomenon, n (%)	99 (19.1)	88 (20.6)	11 (12.0)	0.055
Tobacco use ever, n (%)	153/368 (41.6)	132/300 (44.0)	21/68 (30.9)	0.048
Alcohol use, n (%)	14/354 (4.0)	12/288 (4.2)	2/66 (3.0)	1.00
Follow-up ≥6 months, n (%)	498 (96.0)	412 (96.5)	86 (93.5)	0.237
Follow-up duration, y, median (Q1-Q3)	9.2 (3.9-16.9)	9.9 (4.6-17.9)	6.2 (2.3-13.7)	<0.001

AIHA: Autoimmune hemolytic anemia, APS: Antiphospholipid syndrome, DLE: Discoid lupus erythematosus, SD: Standard deviation

As for autoantibody profiles, antinuclear antibody positivity was around 95% in both groups (Table 2). Antibodies to ribonucleoprotein (anti-RNP) was detected more frequently in patients with adult-onset SLE than in patients with late-onset SLE (24.7% *vs.* 7.1%, p<0.001), whereas anti-Ro52 antibodies were more commonly seen in patients with late-onset SLE which did not reach statistical significance (16.6% *vs.* 24.7%, p=0.079).

Treatment characteristics of the cohort were demonstrated in Table 3. The rate of glucocorticoid use ever was similar in both groups; however, pulse steroids were administered more frequently to the adult-onset SLE patients (19.2% *vs.* 10.9%, p=0.058). In line with the latest finding, when glucocorticoids were grouped according to the maximum dose used during the entire follow-up, the difference reached statistical significance (Table 3). In addition, the patients with adult-onset SLE were more commonly initiated on immunosuppressive agents, which was statistically significant for cyclophosphamide, azathioprine and mycophenolic acid.

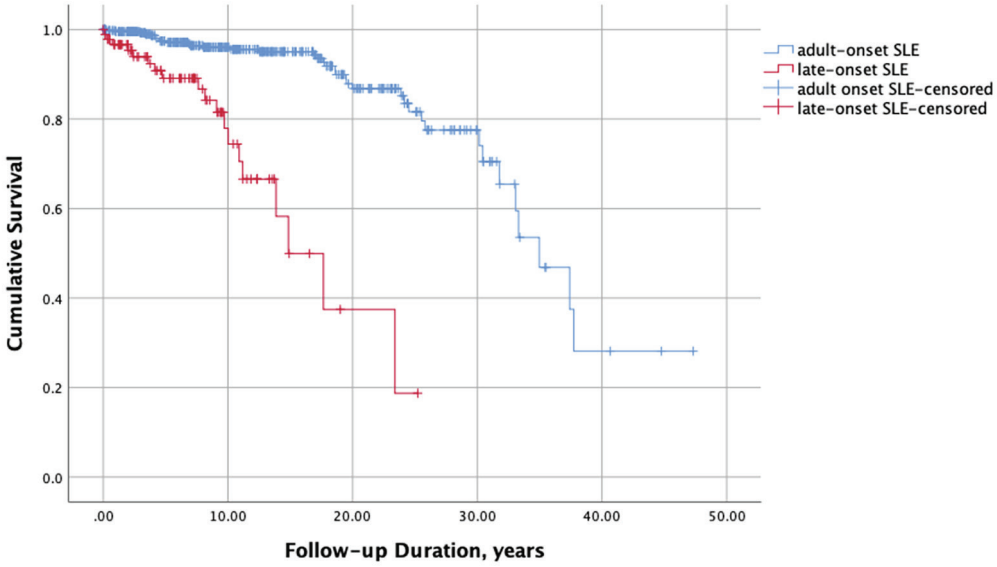

Figure 1. Kaplan-Meier curve of adult-onset and late-onset SLE patients
SLE: Systemic lupus erythematosus

Table 2. Laboratory characteristics of the study population

	All cohort (n=519)	Adult-onset (n=427)	Late-onset (n=92)	p
ANA positivity, n (%)	496/517 (95.9)	409/425 (96.2)	87/92 (94.6)	0.558
Anti-dsDNA positivity, n (%)				0.213
ULN	91/509 (17.9)	78/418 (18.7)	13/91 (14.3)	
>2xULN	234/509 (46.0)	196/418 (46.9)	38/91 (41.8)	
Anti-RNP, n (%)	97/453 (21.4)	91/368 (24.7)	6/85 (7.1)	<0.001
Anti-Sm, n (%)	111/454 (24.4)	95/369 (25.7)	16/85 (18.8)	0.181
Anti-histon, n (%)	79/453 (17.4)	62/368 (16.8)	17/85 (20.0)	0.490
Anti-SS-A, n (%)	167/453 (36.9)	135/368 (36.7)	32/85 (37.6)	0.868
Anti-SS-B, n (%)	54/453 (11.9)	40/368 (10.9)	14/85 (16.5)	0.151
Anti-Ro52, n (%)	82/453 (18.1)	61/368 (16.6)	21/85 (24.7)	0.079
Anti-nucleosome, n (%)	96/453 (21.2)	76/368 (20.7)	20/85 (23.5)	0.559
Anti-ribosomal-P, n (%)	23/453 (5.1)	20/368 (5.4)	3/85 (3.5)	0.593
APA positivity, n (%)				
Lupus anticoagulant, n (%)	97/287 (33.8)	86/245 (35.1)	11/42 (26.2)	0.259
Anti-cardiolipin	41/413 (9.9)	39/343 (11.4)	2/70 (2.9)	0.030
Anti-beta-2 glycoprotein	43/347 (12.4)	36/291 (12.4)	7/56 (12.5)	0.979
Low complement, n (%)	145/516 (28.1)	329/425 (77.4)	42/91 (46.2)	<0.001
Low C3, n (%)	330/515 (64.1)	292/424 (68.9)	38/91 (41.8)	<0.001
Low C4, n (%)	211/516 (40.9)	189/425 (44.5)	22/91 (24.2)	<0.001
Direct coombs test, n (%)	129/176 (73.3)	102/143 (71.3)	27/33 (81.8)	0.220

ANA: Antinuclear antibody, Anti-dsDNA: Anti-double stranded DNA, Anti-RNP: Anti-ribonucleoprotein, Anti-Sm: Anti-Smith, APA: Antiphospholipid antibody, C3: Low complement 3, C4: Low complement 4, ULN: Upper limit of normal

Prognosis and Mortality

The SDI was determined in 498 patients whose follow-up duration was ≥6 months. Of 498 patients, damage accrual was present in 209 (40.3%) patients after median follow-up of 9.4 years. Mean and median damage scores in the study population were 0.94 (SD: 1.51) and 0 (Q1-Q3: 0-1), respectively. There were no differences in terms of damage domains and the SDI scores between two groups (Table 4). The most common damage observed was the musculoskeletal domain (11.8%) followed by renal complications (10.6%). The percentage of malignancy was higher in the late-onset group compared to the adult-onset group (8.1% *vs.* 3.6%, respectively, p=0.081). Interestingly, as demonstrated in Table 1, tobacco use, a well-known risk

Table 3. Treatment characteristics of the study population

	All cohort (n=519)	Adult-onset (n=427)	Late-onset (n=92)	p
Glucocorticoids ever, n (%)	472 (90.9)	392 (91.8)	80 (87.0)	0.142
Pulse steroid ever, n (%)	92 (17.7)	82 (19.2)	10 (10.9)	0.058
Prednisolone dose, n (%)				<0.001
Never	48 (9.2)	35 (8.2)	13 (14.1)	
0-7.5 mg/day	74 (14.3)	53 (12.4)	21 (22.8)	
7.5-19 mg/day	106 (20.4)	84 (19.7)	22 (23.9)	
20-39 mg/day	67 (12.9)	49 (11.5)	18 (19.6)	
40-59 mg/day	78 (15.0)	72 (16.9)	6 (6.5)	
≥60 mg/day	146 (28.1)	134 (31.4)	12 (13.0)	
Antimalarials, n (%)	491 (94.6)	405 (94.8)	86 (93.5)	0.611
NSAIDs, n (%)	192 (37.0)	158 (37.0)	34 (37.0)	0.993
Immunosuppressants, n (%)	343 (66.1)	296 (69.3)	47 (51.1)	0.001
Cyclophosphamide, n (%)	108 (20.8)	101 (23.7)	7 (7.6)	0.001
Rituximab, n (%)	25 (4.8)	23 (5.4)	2 (2.2)	0.283
IVIG, n (%)	42 (8.1)	36 (8.4)	6 (6.5)	0.542
Azathioprine, n (%)	246 (47.4)	218 (51.1)	28 (30.4)	<0.001
Methotrexate, n (%)	61 (11.8)	49 (11.5)	12 (13.0)	0.672
Mycophenolic acid, n (%)	140 (27.0)	129 (30.2)	11 (12.0)	<0.001
Cyclosporin-A, n (%)	25 (4.8)	24 (5.6)	1 (1.1)	0.101
Acetylsalicylic acid, n (%)	206 (39.7)	172 (40.3)	34 (37.0)	0.554
Anticoagulation, n (%)	93 (17.9)	82 (19.2)	11 (12.0)	0.100
Statin use, n (%)	49 (9.4)	36 (8.4)	13 (14.1)	0.090

IVIG: Intravenous immunoglobulin, NSAIDs: Non-steroidal anti-inflammatory drugs

factor for malignancy development, was more common in patients with adult-onset SLE (44.0% *vs.* 30.9%, p=0.048). The most common malignancy was head and neck cancers (22.7%). Among 21 patients with less than 6-month follow-up, 3 patients died prematurely within the 6-month period after SLE diagnosis [2 patients in late-onset SLE group (haemophagocytic syndrome and acute hepatic failure) and 1 patient in adult-onset SLE group (sepsis)].

After median of 9.2 years, 56 out of 519 (10.8%) patients died; 8.7% in the adult-onset SLE and 20.7% in the late-onset SLE (p=0.001). The primary cause of death was infections, accounting for 30.4%, followed by active disease and other causes, each at 14.3%, and cardiac reasons at 5.4%. Twenty patients had an unknown cause of death. The distribution of causes was similar between both groups (data not shown). The 5-year and 10-year survival rates in the cohort were 96% and 93%, respectively. The survival differed between two groups (Log-rank<0.001, see Figure 1). Older age at SLE onset was independently associated with overall mortality in Cox regression analysis when adjusted for sex, SDI score and immunosuppressive use [HR 1.09 (1.06-1.11), p<0.001]. A model, in which smoking was also added as a covariate, HR of age was determined as 1.10 (1.05-1.52).

Discussion

This study found that most of the patients experienced disease onset between the ages of 18 and 49, as expected. The adult-onset group showed higher rates of malar rash as well as renal and neurological involvement, aligning with findings in the published literature.[4,7,11,12] As a consequence, the use of more potent immunosuppressive agents, such as cyclophosphamide, azathioprine and mycophenolate mofetil, were more frequent in patients with adult-onset SLE, which also supports the results of previous studies.[4,11]

Similar to our findings, a systematic review and meta-analysis on the neuropsychiatric manifestations of SLE found that the cumulative frequency of neurological involvement is higher in early-onset SLE patients.[13] Additionally, some studies suggest that anti-RNP antibodies may have an impact on the development of neuropsychiatric symptoms in patients, compared to those without these antibodies.[14,15] Notably, in our study, anti-RNP antibodies were more common in patients with adult-onset SLE than the late-onset SLE patients, potentially indicating a link between these antibodies and neurological involvement. Nevertheless, more research is needed to fully understand the extent of this relationship and the mechanisms through which anti-RNP antibodies influence the neurological aspects of SLE.

Table 4. The SDI domains in each group

	All cohort (n=498)	Adult-onset (n=412)	Late-onset (n=86)	p
Any damage, n (%)	209 (40.3)	171 (40.0)	38 (41.3)	0.823
Damage score, median, (Q1-Q3)	0 (0-1)	0 (0-1)	0 (0-3)	0.669
Damage score, mean (SD)	0.94 (1.51)	0.93 (1.52)	0.98 (1.46)	0.787
Ocular, n (%)	30 (6.0)	23 (5.6)	7 (8.1)	0.365
Cataract	24 (4.8)	17 (4.1)	7 (8.1)	0.160
Retinal	5 (1.0)	5 (1.2)	0 (0)	0.593
Optic atrophy	1 (0.2)	1 (0.2)	0 (0)	≥0.99
Neuropsychiatric, n (%)	25 (5.0)	21 (5.1)	4 (4.7)	≥0.99
Renal, n (%)	53 (10.6)	40 (9.7)	13 (15.1)	0.139
Pulmonary, n (%)	50 (10.0)	40 (9.7)	10 (11.6)	0.590
Cardiovascular, n (%)	48 (9.6)	39 (9.5)	9 (10.5)	0.775
Peripheral vascular, n (%)	35 (7.0)	31 (4.5)	4 (4.7)	0.343
Gastrointestinal, n (%)	21 (4.2)	16 (3.9)	5 (5.8)	0.384
Muskuloskeletal, n (%)	59 (11.8)	52 (12.6)	7 (8.1)	0.242
Muscle atrophy	2 (0.4)	2 (0.5)	0 (0)	≥0.99
Erosive arthritis	5 (1.0)	5 (1.2)	0 (0)	0.593
Osteoporosis	20 (4.0)	17 (4.1)	3 (3.5)	≥0.99
AVN	39 (7.8)	35 (8.5)	4 (4.7)	0.227
Skin, n (%)	5 (1.0)	4 (1.0)	1 (1.2)	≥0.99
Gonadal failure, n (%)	8 (1.6)	8 (1.9)	0 (0)	0.362
Diabetes, n (%)	28 (5.6)	22 (5.3)	6 (7.0)	0.605
Malignancy, n (%)	22 (4.4)	15 (3.6)	7 (8.1)	0.081
Death*, n (%)	53 (10.6)	36 (8.7)	17 (19.8)	**0.003**

**In patients with a follow-up duration ≥6 months*

ACR: American College of Rheumatology, AVN: Avascular necrosis, SD: Standard deviation, SDI: SLICC/ACR damage index, SLICC: Systemic Lupus International Collaborating Clinics

A recently published large cohort study showed that pulmonary embolism and deep vein thrombosis were more frequent in patients with late-onset SLE, where lupus anticoagulant positivity was significantly higher.[11] However, in our study, the percentages of thrombotic events were similar between the groups. Additionally, although the presence of anti-cardiolipin antibodies was statistically higher in the adult-onset group, the occurrence of antiphospholipid antibody syndrome did not differ, remaining at 12.7% in the entire study population. We also found a trend toward high frequency of Raynaud phenomenon in the adult-onset SLE, which was also demonstrated in a large population of Latin American patients with SLE.[4]

Higher SDI scores have been linked to increased rates of morbidity and mortality, and a recent systematic review and meta-analysis has reaffirmed this association.[16] Despite the availability of more targeted therapies in rheumatology and decreased rates of mortality in SLE patients over time,[17] damage still remains a significant challenge in the course of SLE. A long-term follow-up study from the UK indicated that 77% of SLE patients experienced damage accrual. [18] The SLICC inception cohort demonstrated that age, African ethnicity, high disease activity, and hypertension are factors associated with damage accrual.[19] In addition, results from the Hopkins Lupus Cohort demonstrated that the use and dosage of glucocorticoids are associated with damage accrual, and reducing the dosage may lower the estimated risk of organ damage.[20] Another retrospective multicentre European cohort study showed that patients with a disease onset at age ≥50 years had higher mean damage scores compared to pediatric and adult-onset groups.[21] It is worth noting that 40% of our study cohort showed damage and had similar SDI scores in both groups. This may be due to the shorter follow-up duration in the late-onset SLE patients or might suggest a delay in SLE diagnosis in terms of calendar days. Nevertheless, we observed higher mortality rates in the late-onset SLE patients, even after adjusting for sex, SDI scores, and immunosuppressant use, which aligns with the literature.[3,4,11]

Study Limitations

The major limitation of the current study is its retrospective design. Additionally, since we did not have disease activity scores, we were unable to incorporate them into our analyses. Furthermore, we opted to exclude the

childhood-onset group, which was necessary due to the lack of complete follow-up for all pediatric patients, including those lost to follow-up or who died before the age of 18. The absence of comprehensive data for this group could have skewed the overall analysis. Consequently, we believe the results of this study are more generalizable to patients diagnosed at 18 years or older.

Conclusion

In conclusion, this study demonstrates that age at onset significantly impacts clinical presentations and outcomes in SLE patients. Adult-onset SLE tends to present with more severe manifestations, while patients with late-onset SLE had a lower survival rate compared to those with adult-onset SLE, despite generally high survival rates across the cohort. Older age at the time of SLE diagnosis was an independent factor for worse survival, showing that age at onset is important in predicting outcomes. These findings underscore the importance of considering age of onset in disease management, which could ultimately aid in developing more targeted and effective therapeutic strategies tailored to the unique needs of each age group.

Ethics

Ethics Committee Approval: We obtained approval from the Ethics Committee of Ankara University (approval number: İ9-592-21, date: 21.10.2021) and conducted the study in accordance with the Declaration of Helsinki.

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: D.Ş., E.U., N.G-G., M.L.Y., E.G.A-G., M.E.Y., T.M.T., G.K., A.A., Concept: T.M.T., G.K., A.A., Design: D.Ş., T.M.T., G.K., A.A., Data Collection and Processing: D.Ş., B.B., E.U., N.GG., G.T., M.K., M.L.Y., E.G.A-G., M.E.Y., Analysis or Interpretation: D.Ş., E.U., M.E.Y., T.M.T., G.K., A.A., Literature Search: D.Ş., B.B., E.U., M.E.Y., T.M.T., G.K., A.A., Writing: D.Ş., A.A.

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