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Association of African-American Ethnicity and Smoking Status with Total and Individual Damage Index in Systemic Lupus Erythematosus

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Abstract

Introduction—Smoking has been associated with increased incidence, severity of cutaneous lupus, and lupus activity. We looked at the association of both smoking and ethnicity with the individual damage items from the SLICC/ACR Damage Index.

Methods—Poisson regression was used to model the total SLICC/ACR Damage Index score against ever smoking. Cox regression was used to assess the relationship between time to individual damage items and ever smoking. Furthermore, we compared SLICC/ACR Damage Index items among African-American and Caucasian ever smokers.

Results—The study included 2629 patients, 52.6% Caucasian and 39.3% African-American. The prevalence of ever smokers was 35.8%. There was no significant difference in total SLICC/ACR Damage Index score between ever smokers and never smokers after adjustment for ethnicity, gender, age at diagnosis, and years of education. Ever smokers had more atherosclerotic cardiovascular damage and skin damage compared to non-smokers. Caucasian SLE patients who ever smoked were more likely to have muscle atrophy and atherosclerosis compared to Caucasian non-smokers. African-American patients who ever smoked were more likely to have skin damage compared to African-American non-smokers. African-Americans who smoked were more likely to have many more damage items (cataract, renal damage, pulmonary hypertension, cardiomyopathy, deforming or erosive arthritis, avascular necrosis, skin damage, and diabetes) compared to Caucasians who smoked.

Conclusion—Our analysis proved the major effect of smoking on cardiovascular and cutaneous damage. Surprisingly, cardiovascular damage items had higher hazard ratios in Caucasian smokers than non-smokers while skin damage items hazard ratios were higher in African-American smokers compared to non-smokers.

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Conflict of interest

The authors have no potential conflict of interest with respect to the research, authorship, and/ or publication of this article.

Ethics approval

All patients gave written informed consent before taking part in the Hopkins Lupus Cohort. The Johns Hopkins University School of Medicine Institutional Review Board approved the Hopkins Lupus Cohort on an annual basis.

Keywords

Systemic lupus erythematosus; SLICC/ACR Damage Index; Smoking; Ethnicity

Introduction

Organ damage, measured by the Systemic Lupus Erythematosus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index (SDI) [1, 2], is closely associated with increased morbidity and mortality in patients with SLE [3–5]. Previous clinical studies have established high age at diagnosis, male gender, African-American ethnicity, low income, low education level, and corticosteroid use as factors contributing to organ damage in SLE patients [5–7].

In SLE, smoking increased lupus incidence [8–12], severity of cutaneous lupus [13–17], and lupus activity [14, 18, 19]. Response to hydroxychloroquine [13, 20–23] and belimumab [24, 25] was decreased in smokers compared to non-smokers, particularly mucocutaneous manifestations. Smoking rates are higher in African-Americans, in the United States [26]. Several studies have looked at the association between smoking and SLICC/ACR Damage Index scores [7, 18, 27–29]. Three studies exclusively evaluated the effect of smoking on cutaneous damage with conflicting conclusions [14, 19, 29]. Ward et al studied 160 patients from an inception cohort, predominantly African-American, at Duke University and showed that progression to end-stage renal disease in lupus nephritis was more rapid among smokers. The median time to end-stage renal disease among smokers was 145 months compared to greater than 273 months in non-smokers [30]. In an analysis of the LUMINA cohort, a multi-ethnic cohort of around 500 SLE patients, patients who smoked had an increased risk of vascular events which included cardiovascular, cerebrovascular, and peripheral vascular events compared to patients who did not smoke [31].

SLE manifestations and outcomes are known to be affected by ethnicity. Not only does the African-American population have a higher incidence and prevalence of SLE [32, 33] but also more severe clinical manifestations, particularly discoid rash and nephritis [32–34], higher disease activity [35] and damage [36] compared to Caucasians.

The literature lacks large, longitudinal cohort studies that evaluate the effects of smoking on organ damage in SLE patients in different ethnicities. We determined the association between smoking status on total, as well as individual, damage items in SLE. The Hopkins Lupus Cohort, consisting predominantly of Caucasian and African-American patients, allowed us to look at the role of African-American ethnicity.

Methods

The Hopkins Lupus Cohort

The Hopkins Lupus Cohort is a longitudinal cohort of patients diagnosed with SLE at the Hopkins Lupus Center. The cohort was established in 1987 and has been approved by the Johns Hopkins University School of Medicine Institutional Review Board on a yearly basis. All patients gave written informed consent. Data were collected prospectively during

participation in the Hopkins Lupus Cohort during quarterly visits, by protocol. At cohort entry, a detailed clinical history was obtained.

The SLICC/ACR Damage Index (SDI)

SLICC/ACR Damage Index is a validated tool that was developed to measure damage, defined as irreversible organ dysfunction, present for 6 months or longer, regardless of etiology, in all organ systems [1, 2]. The SDI was calculated based on organ damage that occurred after diagnosis with SLE until the last visit. The dependent variable was time from SLE diagnosis to a damage event.

Smoking status

The smoking status was obtained from the patient and updated at each patient visit. In our analysis we looked at ever (past or current) versus never smoking status. There was no quantification of cigarette use available in the cohort database.

Demographic variables

The demographic factors included age at diagnosis, gender, ethnicity, education and annual household income. Education was categorized into less or equal to 12 years and more than 12 years. Income was measured as total annual household income at first visit, falling into 3 categories <\$30,000, \$30,000-\$65,000 and >\$65,000.

Statistical analysis

The chi-square test was used to explore the difference in patient characteristics between ever smokers and non-smokers. Poisson regression was used to model the total SLICC/ACR Damage Index score against ever smoking. Cox regression was used to assess the relationship between time to individual damage items and ever smoking. We also looked at this relationship separately for African-American patients and Caucasian patients. The adjusted hazard ratio (HR) and 95% confidence intervals were reported. For each damage item, patients who had a damage diagnosis prior to SLE diagnosis were excluded in the analysis.

Results

The study included 2629 patients. Of these patients, 92.1% were female, 52.6% Caucasian and 39.3% African-American. The mean age at SLE diagnosis was 32.3 years. Fifty percent of the patients were diagnosed with SLE under the age of 30 years, 32.8% between the age of 30–44, 13.7% between the age of 45 and 59, and 3.5% diagnosed at the age of 60 and over. The prevalence of smoking was 35.8% for all cohort patients, 36.0% in African-American patients and 38.1% in Caucasian patients. Smokers had lower education, lower income levels, and higher prevalence of alcohol and drug use. Patient sociodemographic characteristics are detailed in Table 1.

Using a Poisson regression model we showed that smokers did not have increased total damage compared to non-smokers after adjusting for gender, ethnicity, age at diagnosis, and education (HR= 1.03, p-value= 0.5172). This was true as well after stratification for

ethnicity: African-American (HR= 1, p- value= 0.9922) vs. Caucasians (HR= 1.06, p- value = 0.3643).

Table 2 shows the cox regression results to assess the relationship between time to SLICC/ACR Damage Index items and smoking. We first compared ever smokers to non-smokers in the entire cohort. We then looked at this relationship separately for African-American patients and Caucasian patients. Adjusted hazard ratios (HR) and 95% confidence intervals were reported. Smoking was an independent predictor for coronary artery disease (angina or coronary artery bypass and myocardial infarction), claudication, and skin damage. After stratification by ethnicity, Caucasians who ever smoked were at higher risk of coronary artery disease and muscle atrophy compared to non-smokers. Gonadal failure in Caucasians was near significance. In African-American patients, smoking remained an independent predictor of any cutaneous damage (particularly extensive scarring). There was an inverse relationship between smoking and cranial or peripheral neuropathy, pulmonary fibrosis and osteoporosis in African-American patients.

Table 3 shows the comparison between African-American smokers and Caucasian smokers regarding time to SLICC/ACR Damage Index items. African-American smokers were at higher risk of cataract, renal damage, pulmonary hypertension, cardiomyopathy, deforming or erosive arthritis, avascular necrosis, skin damage, and diabetes compared to Caucasian smokers. However, African-American smokers were less likely to have infarction or resection of bowel and osteoporosis with fracture or vertebral collapse compared to Caucasian smokers.

Discussion

This study is the largest cohort study to date evaluating the effect of smoking on the cumulative SLICC/ACR Damage Index and its individual damage items. It is the only study that examined the effect of smoking on individual items of the SLICC/ACR Damage Index in terms of Caucasians vs. African-American ethnicity. In contrast with the general U.S. population, African-Americans in the cohort did not have a higher frequency of smoking than Caucasians.

First, surprisingly, we found that ever smokers did not have higher total SLICC/ACR Damage Index scores compared to non-smokers. This is in agreement with Ekblom-Kullberg et al, who found that smokers and non-smokers not only had comparable SLICC/ACR Damage Indices, but also that current smokers had lower disease activity and lower anti-dsDNA levels [37]. In our cohort, however, smoking was not associated with higher anti-dsDNA or mean SLEDAI scores (p-values=0.7680, 0.9100 respectively). Turchin et al and Kim et al also did not find any association between total SLEDAI-2K nor total Damage Index scores in current smokers compared to non-smokers in predominantly Caucasian and Asian cohorts respectively [14, 29]. In mice, Rubin et al showed a negative association between smoking and anti-DNA and anti-chromatin IgG levels [38]. This was confirmed by extending the study to newly diagnosed SLE patients on no treatment [38]. These studies suggested an immunosuppressive role of nicotine through its effect on T cell ability to transmit antigen-receptor-mediated signals [39].

On the other hand, studies by Legge et al and Montes et al (evaluating total damage in Caucasian and Brazilian SLE patients, respectively), found an association between smoking and total SLICC/ACR Damage Index [7, 28] (p-values=0.02 in both studies). Ghaussy et al, analyzing 111 patients predominantly of Hispanic ethnicity, found a non-significant trend towards higher cumulative damage in current smokers (SDI scores were 4.34 ± 2.41 , 3.89 ± 2.68 , and 3.60 ± 2.85 for current, ex-, and never smokers, respectively) [18]. In this same study, the mean SLEDAI score was higher in current smokers compared to former and non-smokers [18]. In a study which included only Caucasian SLE patients, higher titers of anti-dsDNA was observed in smokers compared to non-smokers [40].

Second, in this study, we demonstrate that smoking was associated with an increased risk of coronary artery disease and peripheral arterial disease. A past analysis, of a subset of our cohort in the atorvastatin intervention trial, showed that smoking was an independent predictor of atherosclerosis progression [41]. In the LUMINA cohort, patients who had arterial thrombotic events (myocardial infarction, angina, coronary artery bypass graft surgery, stroke, claudication, gangrene, or tissue loss and/or peripheral arterial thrombosis) were more likely to be smokers [42].

Third, smoking worsened cutaneous damage. Our study is in agreement with other studies that demonstrated that smoking worsened cutaneous damage [14]. In fact, several studies identified smoking as a trigger for skin manifestations, mainly discoid lupus [13, 17, 34]. Moreover, smoking appears to decrease the efficacy of hydroxychloroquine in a dose-dependent fashion, particularly in cutaneous lupus [13, 20–23]. Turchin et al demonstrated that current smokers had trends towards higher lupus cutaneous activity, largely driven by the specific type of active lupus rash [14]. More cutaneous manifestations and poorer response to antimalarial treatment are valid explanations for the greater cutaneous damage in smokers.

Fourth, although ethnicity has been identified as a risk modifier in the burden of tobacco-related diseases [43], our study is the first to show the differential effect of smoking on the SLICC/ACR Damage Index items depending on the ethnicity of SLE patients. This is in support of possible gene-environment interactions in altering the effect of cigarette smoking on clinical and serologic phenotypes. African-American smokers had many more damage items compared to Caucasian smokers. Among smokers, African-Americans were at higher risk of cataract, renal damage, pulmonary hypertension, cardiomyopathy, deforming or erosive arthritis, avascular necrosis, skin damage, and diabetes, whereas there was only a higher risk of osteoporosis with fracture and gastrointestinal infarction in Caucasian smokers.

Fifth, smoking had a greater effect on skin damage in African-American patients. In contrast, Caucasians who ever smoked had higher hazard ratios of atherosclerotic and arterial thrombotic damage compared to non-smokers. SLE patients who ever smoked had a 3-fold increase in cardiovascular events compared to nonsmokers [31]. In a prospective study, African-American patients were at an increased risk of cardiovascular events compared to Caucasians [44]. The differential effect of smoking in Caucasians observed in our study has never been reported before.

Sixth, Caucasian ever smokers were more likely to have muscle atrophy compared to Caucasian non-smokers. The association between long-term smoking and muscle atrophy, in the general population, is well established [45]. Moreover, a study of 465 patients with polymyositis, showed that Caucasian ever-smokers were more likely to have polymyositis, compared to never-smokers. This association was not statistically significant in African-Americans [46].

Seventh, studies in the general population found any exposure to tobacco (current, ever and second hand smoking) was associated with an increased risk of infertility and early menopause [47]. In our study, the effect of smoking on gonadal failure was close to significance only in Caucasians.

Eight, smoking was actually protective against some types of organ damage. Our findings suggest that there is a relationship between smoking and lower risk of cranial neuropathy in African-American patients. This finding is surprising, as it is well-known that smoking increases the risk of neuropathy in diabetic patients [48]. Epidemiologic studies have found an inverse relationship between smoking and Parkinson's disease. The protective effect is thought to be explained by the effects of nicotine on the dopaminergic system. We have no explanation for the protective effect in SLE.

Moreover, there was an inverse relationship between smoking and pulmonary fibrosis in African-American patients. In the general population, only a fraction of chronic smokers develop chronic lung disease. The proteomes of lungs from chronic smokers, non-smokers, and ex-smokers were evaluated in one study [49]. There was an upregulation of unfolded protein response in smokers. Unfolded protein response is responsible for inducing proteins responsible for protection against antioxidant injury and inflammation [49]. Upregulation of such a response is a possible explanation of the protective role of smoking on pulmonary fibrosis in African-Americans.

Ninth, we failed to find an association between smoking and renal damage, osteoporotic fractures, and cataract in our patients. Smokers were not at higher risk of developing kidney damage. This is in harmony with our past report that did not find an association between smoking and renal insufficiency and renal failure [50]. McAlindon et al also did not find that smokers were at a higher risk of glomerulonephritis [51]. Ward et al, however, demonstrated that the median time to end-stage renal disease among smokers was 145 compared to greater than 273 months in non-smokers (p-value= 0.04) [30].

A previous report from our cohort showed that current and ever smoking status was associated with increased musculoskeletal damage [52]. We did not find an association between smoking and osteoporosis or avascular necrosis in this larger sample. Cataract is the most common ocular damage in SLE patients [53]. Despite its known association in the general population, smoking was not a risk factor for cataract in our SLE patients. This is in agreement with a previous analysis of modifiable risk factors associated with cataract in our cohort [53].

The strengths of our study include the large sample size that allowed us to evaluate the effect of smoking on individual SLICC/ACR Damage Index items. Our study does have limitations

and potentials for bias, as we studied only a single aspect of smoking (ever versus never smoker), we could not take into account second hand smoking, and did not quantify smoking.

Conclusion

Smoking did not increase the total SLICC/ACR Damage Index in SLE. Our analysis proved the major effect of smoking was on cardiovascular damage (angina, coronary bypass, myocardial infarction and claudication) and cutaneous damage. There was a differential effect of smoking according to ethnicity. Cardiovascular damage items had higher hazard ratios in Caucasian smokers. Extensive cutaneous scarring hazard ratios were higher in African-American smokers. African-American smokers had more items of organ damage than Caucasian smokers.

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Key points

1. This study is the largest cohort study to date evaluating the effect of smoking on the cumulative SLICC/ACR Damage Index and its individual damage items.
2. It is the only study that examined the effect of smoking on individual items of the SLICC/ACR Damage Index in terms of Caucasians vs. African-American ethnicity.
3. Our analysis proved the major effect of smoking on cardiovascular and cutaneous damage. Compared to non-smokers, Caucasian smokers had higher risk of cardiovascular damage while African-American smokers had more skin damage.
4. African-Americans who smoked were more likely to have many more damage items (cataract, renal damage, pulmonary hypertension, cardiomyopathy, deforming or erosive arthritis, avascular necrosis, skin damage, and diabetes) compared to Caucasians who smoked.

Table 1:

Patient sociodemographic characteristics of the Hopkins Lupus Cohort by smoking status

	All (n=2629)			African American (n=1033)			Caucasian (n=1382)		
	Ever smokers	Never smokers	p-value	Ever smokers	Never smokers	p-value	Ever smokers	Never smokers	p-value
Gender			0.0003			0.0026			0.2282
Female	89.6%	93.5%		90.3%	95.1%		89.8%	91.8%	0%
Male	10.4%	6.5%		9.7%	4.9%		10.2%	8.3%	
Age at SLE diagnosis			<0.0001			<0.0001			<0.0001
<30 years	39.7%	55.8%		39.7%	57.2%		39.1%	52.4%	
30–44 years	36.7%	30.7%		38.4%	32.9%		35.7%	30.6%	
45–59 years	17.7%	11.4%		17.6%	9.2%		17.9%	14%	
60+ years	5.9%	2%		4.3%	0.8%		7.3%	3.1%	
Education			<0.0001			<0.0001			<0.0001
12 years	47.6%	24.9%		58.1%	31.3%		42.4%	21.0%	
>12 years	52.4%	75.1%		41.9%	68.7%		57.6%	79.0%	
Family income			<0.0001			<0.0001			0.0002
< \$30,000	41.6%	25.7%		64.1%	40.7%		26.2%	17%	
\$30,000–\$65,000	29.9%	34.2%		24.1%	31.8%		35.4%	35.9%	
\$ 65,000+	28.5%	40.2%		11.8%	27.5%		38.4%	47.1%	
Insurance			<0.0001			<0.0001			0.0001
Private	71.8%	82.2%		56.4%	70.6%		82.9%	90.8%	
MA	24.8%	15.6%		38.4%	26.1%		15.1%	8.3%	
None	3.4%	2.2%		5.3%	3.3%		2%	0.9%	
Marital status			<0.0001			<0.0001			0.0006
Married	52.2%	54.1%		30.5%	39.2%		67.3%	64.7%	
Single	28.5%	35.4%		43.3%	48.4%		17.2%	25.6%	
Separated	3.6%	2.4%		5.5%	3.4%		2.3%	1.6%	
Widowed	3.6%	1.8%		6%	2.6%		2.1%	1.4%	
Divorced	12.2%	6.2%		14.7%	6.4%		11.1%	6.8%	
Alcohol abuse			<0.0001			<0.0001			<0.0001
Ever	14.8%	2.2%		21.6%	1.7%		11%	2.6%	
Never	85.2%	97.9%		78.4%	98.3%		89%	97.4%	
Drug abuse			<0.0001			<0.0001			<0.0001
Ever	14.5%	1.6%		21.4%	1.7%		10%	1.5%	
Never	85.5%	98.4%		78.7%	98.3%		90%	98.5%	

Table 2:

Associations of time to SLICC/ ACR Damage Index items and smoking status in all cohort patients and separately in African- American and Caucasian patients (stratification by ethnicity)

	# of events	All	p-value	# of events	African American	p-value	# of events	Caucasian	p-value
		HR ¹ (95% CI)			HR ² (95% CI)			HR ² (95% CI)	
Any cataract ever	420	1 (0.82,1.22)	0.9948	172	1.3 (0.95,1.78)	0.0979	229	0.77 (0.59,1.02)	0.0652
Retinal change OR optic atrophy	103	0.91 (0.61,1.36)	0.6389	42	0.85 (0.45,1.61)	0.6133	58	0.86 (0.51,1.49)	0.5988
Cognitive impairment OR major psychosis	135	1.09 (0.76,1.56)	0.6301	51	0.69 (0.38,1.28)	0.2434	78	1.22 (0.77,1.92)	0.4055
Seizures requiring therapy for 6 months	62	0.93 (0.54,1.62)	0.8047	24	0.65 (0.26,1.66)	0.3700	32	0.98 (0.46,2.06)	0.9505
Cerebral vascular accident ever OR resection	186	1.08 (0.8,1.47)	0.6012	85	1.08 (0.69,1.7)	0.7219	94	1.02 (0.66,1.56)	0.9427
Cranial OR peripheral neuropathy	186	0.85 (0.63,1.16)	0.3046	71	0.49 (0.29,0.83)	0.0081	109	1.24 (0.84,1.83)	0.2749
Transverse myelitis	16	0.51 (0.14,1.84)	0.3030	7	0.64 (0.12,3.59)	0.6158	8	0.38 (0.05,3.07)	0.3609
Estimated or measured GFR < 50%	447	0.94 (0.77,1.15)	0.5640	220	1.03 (0.78,1.36)	0.8484	193	0.82 (0.6,1.1)	0.1821
Proteinuria 3.5g/24hrs	179	0.95 (0.68,1.31)	0.7379	103	1.11 (0.72,1.7)	0.6390	53	0.79 (0.43,1.45)	0.4470
End-stage renal disease	120	0.72 (0.48,1.07)	0.1060	74	0.82 (0.49,1.35)	0.4285	37	0.57 (0.26,1.24)	0.1550
Pulmonary hypertension	190	1.19 (0.89,1.6)	0.2485	107	1.33 (0.89,1.98)	0.1593	76	0.95 (0.59,1.5)	0.8119
Pulmonary fibrosis	178	0.77 (0.56,1.06)	0.1035	89	0.54 (0.34,0.86)	0.0094	81	1.04 (0.66,1.63)	0.8681
Shrinking lung	9	0.34 (0.04,2.8)	0.3192	3	N/C	N/C	6	0.52 (0.06,4.52)	0.5529
Pleural fibrosis	68	0.95 (0.58,1.58)	0.8563	31	0.52 (0.24,1.15)	0.1089	33	1.35 (0.67,2.72)	0.3976
Pulmonary infarction OR resection	8	0.66 (0.13,3.4)	0.6209	1	N/C	N/C	7	0.77 (0.14,4.11)	0.7567
Angina OR coronary artery bypass	88	1.55 (1.2,39)	0.0498	29	1.41 (0.65,3.04)	0.3870	55	1.84 (1.06,3.19)	0.0309
Myocardial infarction ever	99	1.77 (1.17,2.67)	0.0070	43	1.52 (0.8,2.87)	0.2011	50	2.05 (1.16,3.63)	0.0138
Cardiomyopathy	80	1.37 (0.86,2.17)	0.1839	49	1.3 (0.72,2.36)	0.3891	27	1.45 (0.67,3.13)	0.3477
Valvular disease	59	0.87 (0.51,1.5)	0.6245	24	1.4 (0.6,3.25)	0.4406	33	0.62 (0.29,1.31)	0.2114
Pericarditis>6 months, OR pericardiectomy	30	0.85 (0.38,1.89)	0.6901	20	0.41 (0.13,1.29)	0.1287	9	3.15 (0.75,13.14)	0.1158
Claudication x6 months	35	2.87 (1.38,5.97)	0.0047	16	3.36 (1.03,10.96)	0.0440	19	2.54 (0.99,6.55)	0.0529
Minor tissue loss (pulp space)	15	0.64 (0.19,2.12)	0.4662	9	0.73 (0.17,3.22)	0.6826	5	0.46 (0.05,4.28)	0.4975
Significant tissue loss ever	21	1.44 (0.59,3.53)	0.4220	10	1.6 (0.42,6.05)	0.4881	10	1.4 (0.39,4.99)	0.6024
Venous thrombosis with swelling, ulceration, OR venous stasis	66	0.54 (0.31,0.94)	0.0294	26	0.52 (0.22,1.24)	0.1393	40	0.55 (0.27,1.13)	0.1029

	# of events	All HR ¹ (95% CI)	p-value	# of events	African American HR ² (95% CI)	p-value	# of events	Caucasian HR ² (95% CI)	p-value
Infarction or resection of bowel	209	1.06 (0.8,1.42)	0.6694	76	0.74 (0.45,1.22)	0.2370	126	1.22 (0.85,1.76)	0.2790
Mesenteric insufficiency	8	0.68 (0.16,2.98)	0.6083	5	1.09 (0.17,7.02)	0.9253	3	0.54 (0.05,6.2)	0.6241
Chronic peritonitis	7	0.26 (0.03,2.29)	0.2262	4	N/C	N/C	3	1.11 (0.1,12.53)	0.9328
Stricture OR upper gastrointestinal tract surgery ever	16	1.08 (0.39,3.04)	0.8772	9	1.54 (0.39,6.17)	0.5405	7	0.67 (0.12,3.59)	0.6395
Pancreatitis	9	5.47 (1.09,27.42)	0.0386	2	N/C	N/C	7	3.93 (0.73,21.29)	0.1124
Muscle atrophy or weakness	47	1.42 (0.78,2.6)	0.2489	26	0.73 (0.31,1.72)	0.4737	20	2.69 (1.08,6.72)	0.0337
Deforming or erosive arthritis	232	0.83 (0.63,1.09)	0.1759	130	0.76 (0.53,1.11)	0.1562	85	1.05 (0.68,1.63)	0.8283
Osteoporosis with fracture or vertebral collapse	312	0.9 (0.72,1.14)	0.4004	93	0.64 (0.41,0.99)	0.0454	210	1 (0.76,1.32)	0.9978
Avascular necrosis	198	1.24 (0.92,1.67)	0.1636	110	1.41 (0.94,2.11)	0.0991	73	0.95 (0.58,1.56)	0.8411
Osteomyelitis	19	1.21 (0.47,3.08)	0.6946	7	0.96 (0.19,4.8)	0.9555	12	1.48 (0.47,4.73)	0.5042
Ruptured tendon	74	1.25 (0.77,2.01)	0.3645	29	1.66 (0.75,3.69)	0.2137	41	0.72 (0.37,1.43)	0.3511
Scarring chronic alopecia	65	1.6 (0.96,2.67)	0.0713	53	1.51 (0.85,2.66)	0.1561	11	2.57 (0.73,9.11)	0.1432
Extensive scarring or panniculum other than scalp and pulp space	37	2.53 (1.26,5.07)	0.0092	27	2.92 (1.27,6.76)	0.0120	10	1.82 (0.5,6.59)	0.3596
Skin ulceration (not due to thrombosis) for more than 6 months	25	2.7 (1.15,6.35)	0.0225	13	3.17 (0.91,10.98)	0.0690	12	2.31 (0.7,7.57)	0.1681
Premature gonadal failure	67	1.45 (0.87,2.41)	0.1561	26	1.13 (0.49,2.63)	0.7719	32	1.89 (0.92,3.89)	0.0837
Diabetes	134	1.07 (0.75,1.53)	0.6926	79	1.27 (0.8,2.01)	0.3175	50	0.71 (0.39,1.3)	0.2678
Malignancy (exclude dysplasia)	245	0.99 (0.76,1.29)	0.9326	92	0.9 (0.59,1.39)	0.6392	148	1 (0.71,1.4)	0.9902

¹ Adjusted for sex, race, age at diagnosis, years of education² Adjusted for sex, age at diagnosis, years of education

Table 3:

Associations between SLICC/ ACR Damage Index items and ethnicity: comparing African Americans and Caucasians ever smokers

	# of events among smokers	HR ^I (95% CI)	p-value
Any cataract ever	176	1.42 (1.05,1.93)	0.0240
Retinal change OR optic atrophy	40	0.92 (0.48,1.76)	0.7994
Cognitive impairment OR major psychosis	52	0.65 (0.36,1.17)	0.1510
Seizures requiring therapy for 6 months	19	0.82 (0.32,2.14)	0.6896
Cerebral vascular accident ever OR resection	77	1.30 (0.82,2.06)	0.2565
Cranial OR peripheral neuropathy	70	0.62 (0.37,1.04)	0.0676
Transverse myelitis	3	3.70 (0.34,40.79)	0.2858
Estimated or measured GFR < 50%	173	1.82 (1.33,2.48)	0.0002
Proteinuria 3.5g/24hrs	56	2.97 (1.66,5.32)	0.0002
End-stage renal disease	37	3.87 (1.8,8.3)	0.0005
Pulmonary hypertension	86	2.25 (1.44,3.53)	0.0004
Pulmonary fibrosis	60	1.02 (0.61,1.72)	0.9385
Shrinking lung	1	N/C	N/C
Pleural fibrosis	25	0.99 (0.43,2.25)	0.9737
Pulmonary infarction OR resection	2	N/C	N/C
Angina OR coronary artery bypass	48	0.60 (0.33,1.12)	0.1092
Myocardial infarction ever	52	1.03 (0.59,1.81)	0.9111
Cardiomyopathy	39	2.65 (1.34,5.21)	0.0049
Valvular disease	22	1.23 (0.52,2.89)	0.6390
Pericarditis>6 months, OR pericardiectomy	10	0.82 (0.23,2.97)	0.7635
Claudication x6 months	24	1.17 (0.51,2.69)	0.7097
Minor tissue loss (pulp space)	4	3.57 (0.36,35.57)	0.2774
Significant tissue loss ever	11	1.14 (0.34,3.8)	0.8325
Venous thrombosis with swelling, ulceration, OR venous stasis	19	0.81 (0.32,2.07)	0.6635
Infarction or resection of bowel	83	0.56 (0.35,0.89)	0.0143
Mesenteric insufficiency	3	1.83 (0.17,20.21)	0.6226
Chronic peritonitis	1	N/C	N/C
Stricture OR upper gastrointestinal tract surgery ever	7	2.68 (0.5,14.29)	0.2480
Pancreatitis	7	0.61 (0.11,3.23)	0.5596
Muscle atrophy or weakness	21	1.10 (0.46,2.66)	0.8254
Deforming or erosive arthritis	85	1.69 (1.09,2.63)	0.0194
Osteoporosis with fracture or vertebral collapse	120	0.42 (0.28,0.63)	0.0000
Avascular necrosis	76	2.50 (1.54,4.04)	0.0002
Osteomyelitis	9	0.45 (0.11,1.86)	0.2711
Ruptured tendon	29	1.55 (0.72,3.36)	0.2618

	# of events among smokers	HR ^I (95% CI)	p-value
Scarring chronic alopecia	33	4.66 (2.01,10.83)	0.0003
Extensive scarring or panniculum other than scalp and pulp space	23	3.90 (1.44,10.57)	0.0075
Skin ulceration (not due to thrombosis) for more than 6 months	16	1.31 (0.48,3.57)	0.6003
Premature gonadal failure	27	0.64 (0.29,1.42)	0.2712
Diabetes	59	3.12 (1.75,5.54)	0.0001
Malignancy (exclude dysplasia)	99	0.82 (0.55,1.24)	0.3527

^I Adjusted for sex, age at diagnosis, and years of education