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Treatment patterns and control of hypertension in systemic lupus erythematosus (SLE): a cross-sectional study

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ABSTRACT

Objective Hypertension (HTN) is common in systemic lupus erythematosus (SLE), representing a key risk factor for cardiovascular and renal disease. We described HTN treatment patterns in SLE, evaluated uncontrolled HTN according to Canadian and American guidelines and identified factors associated with uncontrolled HTN.

Methods We performed a cross-sectional study, identifying all McGill Lupus Clinic registry patients with an annual visit between January 2017 and May 2019 who were taking HTN medications. We excluded those taking medications only for another indication (eg, Raynaud's). We determined the frequency of uncontrolled HTN according to Canadian and American College of Cardiology/American Heart Association guidelines. Multivariate logistic regression (adjusted for age, sex and race/ethnicity) evaluated if uncontrolled HTN was more common with high body mass index (BMI), longer SLE duration, high disease activity, renal damage, multiple concomitant antihypertensives, prednisone and non-steroidal anti-inflammatory drugs.

Results Of 442 patients with SLE, 108 were taking medications to treat HTN, and 38 took multiple medications concurrently. Angiotensin-receptor blockers were most common, followed by calcium channel blockers, diuretics, angiotensin-converting enzyme inhibitors and beta blockers. Among the 108 patients, 39.8% (n=43) had blood pressure (BP) >140/90 mm Hg, while 66.7% (n=72) had BP >130/80 mm Hg. In multivariate analyses, uncontrolled HTN (>130/80 mm Hg) was more likely in Caucasians (OR 2.72, 95% CI 1.12 to 6.78) and patients with higher BMI (OR 1.08, 95% CI 1.00 to 1.19). Patients with renal damage had better HTN control (OR 0.39, 95% CI 0.16 to 0.97). We could not draw definitive conclusions regarding other variables.

Conclusion Caucasians and patients with higher BMI had more uncontrolled HTN. The negative association with renal damage is reassuring, as controlled BP is key for renal protection.

Strengths and limitations of this study

- Hypertension is a common comorbidity of systemic lupus erythematosus (SLE), therefore understanding and addressing risk factors to suboptimal control is crucial to avoid future cardiovascular and renal consequences.
- Our study was performed on a large cohort of patients with SLE who receive annual standardised evaluations of clinical characteristics.
- Results were computed using multivariate logistic regression analyses adjusted for age, sex and race/ethnicity.
- The cross-sectional nature of our study may only allow for identification of associations.
- Our study was performed in a specialised clinic within a tertiary hospital.

INTRODUCTION

In systemic lupus erythematosus (SLE), hypertension (HTN) is common[1 2] and represents a major, correctable risk factor for cardiovascular disease and renal damage, two frequent adverse outcomes in SLE.[3 4] Certain subgroups with patient with SLE have traditionally had worse disease outcome, including older patients, men, non-Caucasians, those with active disease, high body mass index (BMI) and renal damage.[5–8] To our knowledge, data on risk factors leading to uncontrolled HTN in patients with SLE remain scarce. We conducted an assessment of the McGill University Health Centre Lupus Clinic registry to describe HTN treatment patterns, evaluate the prevalence of uncontrolled HTN according to Hypertension Canada and the more stringent American College of Cardiology/American Heart Association (ACC/AHA) guidelines for HTN and assess uncontrolled HTN in the traditionally vulnerable groups of men, non-Caucasians, older patients with SLE, as well as patients with high BMI, active SLE or renal damage. The effects of prednisone and non-steroidal anti-inflammatory drug (NSAID) use on uncontrolled HTN were also evaluated.

MATERIALS AND METHODS

We conducted a cross-sectional assessment of data extracted from the McGill University Health Centre Lupus Clinic registry. Patients enrolled in the cohort received an SLE diagnosis in accordance to the American College of Rheumatology criteria confirmed by a lupus specialist.[9] Informed written consent was obtained from each patient prior to cohort enrolment. Prospectively collected data include demographics (age, sex, race/ethnicity) and clinical characteristics (SLE disease activity and damage, medications, BMI and other variables) updated during standardised annual assessments where blood pressure (BP) is measured once, seated, with an automated cuff.

We identified all patients between January 2017 and May 2019 taking medications for HTN at the time of their last annual visit. We did not include antihypertensive agents taken for other reasons, such as Raynaud's syndrome and proteinuria. The frequency of use for each class of HTN medication (ie, ACE inhibitors (ACEI), angiotensin II receptor blocker (ARB), calcium channel blocker (CCB), beta-blocker, diuretics) was computed.

We examined the prevalence of uncontrolled HTN within the cohort according to 2017 HTN guidelines from both Hypertension Canada and the ACC/AHA. The 2017 Canadian guidelines recommend a target systolic arterial BP of <140 mm Hg and diastolic arterial BP of <90 mm Hg for cardiovascular disease prevention.[10] Conversely, the more stringent ACC/AHA guidelines target a systolic arterial pressure of <130 mm Hg, and a diastolic arterial pressure of <80 mm Hg.[11]

We analysed characteristics and demographics of patients with uncontrolled HTN, defined using the more stringent ACC/AHA guidelines of a BP surpassing 130/80 mm Hg despite the use of antihypertensive medications, as patients with SLE are at risk of cardiovascular disease. We developed multivariate logistic regression analyses including sex, Caucasian race/ethnicity, age, BMI, SLE disease duration, renal damage, number of current HTN medications, as well as prednisone and NSAID use. Variables also included the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K)[12], a global SLE disease activity index used clinically and in research which measures 24 clinical variables across all systems.[12] The analysis was carried out using the generalised linear model function of the R software. The overall regression diagnosis has been validated by the receiver operating characteristic curve (ROC curve) and the Hosmer-Lemeshow test.

RESULTS

During the study period of January 2017 to May 2019, 442 patients with SLE from the McGill University Health Centre Lupus Clinic registry were assessed. The mean age at assessment was 48 years old, with a mean age at SLE diagnosis of 31 years. Women comprised 87.8% of the cohort. Regarding race/ethnicity, 60.4% were Caucasian, 14.5% black, 13.1% Asian and the remainder (12.0%) of other race/ethnicity. The mean BMI was 26.6.

Of the 442 patients, 108 (24.4%) were currently taking medications to treat HTN, with 38 patients taking multiple antihypertensives concurrently. Angiotensin receptor blockers were most commonly prescribed (N=44), followed by CCB (N=40), diuretics (N=33), ACEI (N=25) and beta-blockers (N=16).

Among the 108 patients taking antihypertensive medications, 39.8% (N=43) had a BP greater than 140/90 mm Hg, representing suboptimal control as per Canadian guidelines. More than two-thirds (66.7%, N=72) of patients on antihypertensive medications had BP greater than 130/80 mm Hg, representing suboptimal control as per ACC/AHA guidelines (table 1).

Renal damage, defined as a Systemic Lupus International Collaborating Clinics (SLICC) renal score ≥1, was present in 21% (N=15) of Caucasian patients taking HTN medications and in 46% (N=17) of patients of another race taking HTN medications.

Multivariate analyses of the 108 patients included sex, race/ethnicity, age at last visit, BMI, SLE duration, disease activity (SLEDAI-2K), renal damage, number of antihypertensive medications, as well as prednisone and NSAID use. Caucasian patients with SLE were more likely to have uncontrolled HTN according to the ACC/AHA definition (OR 2.72, 95% CI 1.12 to 6.78). We noted that higher BMI also was associated with uncontrolled HTN (OR 1.08, 95% CI 1.00 to 1.19). Conversely, patients with renal damage had better BP control (OR 0.39, 95% CI 0.16 to 0.97). The effects of the other variables assessed were not clear as the 95% CIs were wide and included the null value (table 2).

DISCUSSION

HTN is an important contributor to cardiovascular disease, renal damage and death in patients with SLE.[3 4] Prior studies have identified risk factors for HTN onset in SLE,[13] but there are less data assessing risk factors for uncontrolled HTN. In our cohort, 24.4% of patients with SLE were taking medications for HTN. Prior studies have estimated that 33%–48% of patients with SLE take an antihypertensive medication or have a BP measure surpassing 140/90 mm Hg.[2 14 15] Importantly, we found a high prevalence of uncontrolled HTN, with 43 (39.8%) of the 108 patients taking antihypertensive medications having uncontrolled BP according to the Canadian guidelines, and 72 patients (66.7%) according to ACC/AHA guidelines. This finding reinforces the need to examine risk factors contributing to uncontrolled BP in SLE, in order to better manage our patients.

Among the 108 patients from the cohort currently taking antihypertensive medications, the most commonly used medication class were ARBs, followed by CCB, diuretics, ACEI and beta-blockers. There are no specific guidelines for the first-line antihypertensive medication to use in SLE, however ARB and ACEI have been

Table 1 Characteristics of the 108 patients with SLE treated for HTN, controlled versus uncontrolled HTN (>130/80 mm Hg)

Variables	All patients N=108	Controlled, N=36	Uncontrolled, N=72	Differences (95% CI)*
Male sex, N (%)	18 (16.7)	6 (16.7)	12 (16.7)	<0.01 (–0.17 to 0.14)
Caucasian race/ethnicity, N (%)	71 (65.7)	19 (52.8)	52 (72.2)	0.19 (0.00 to 0.38)
Age at last visit >65 years, N (%)	45 (41.7)	12 (33.3)	33 (45.8)	0.12 (–0.07 to 0.30)
Mean body mass index, (SD)	26.6 (5.2)	25.6 (5.1)	27.1 (5.2)	2.04 (–0.42 to 4.17)
Mean SLE duration, years (SD)	23.5 (14.2)	23.1 (15.2)	23.7 (13.8)	0.94 (–5.01 to 6.96)
SLEDAI-2K ≥4, N (%)	48 (44.4)	18 (50.0)	30 (41.7)	0.08 (–0.11 to 0.27)
Renal damage ≥1, N (%)	32 (29.6)	16 (44.4)	16 (22.2)	0.22 (0.04 to 0.40)
Prednisone use, N (%)	16 (14.8)	5 (13.9)	11 (15.3)	0.01 (–0.15 to 0.14)
NSAIDs use, N (%)	5 (4.6)	1 (2.8)	4 (5.6)	0.03 (–0.09 to 0.11)
Using >1 BP medication, N (%)	38 (35.2)	10 (27.8)	28 (38.9)	0.11 (–0.08 to 0.28)
Mean systolic BP, (SD)	134.2 (18.2)	116.0 (9.4)	143.2 (14.3)	26.0 (21.0 to 31.0)
Mean diastolic BP, (SD)	79.9 (10.8)	70.7 (6.3)	84.6 (9.5)	13.0 (10.0 to 16.0)

*The difference in proportions between groups (controlled (n=36) and uncontrolled (n=72)) as well as their 95% CIs. This analysis was performed using the Newcombe-Wilson score method. For continuous variables (body mass index, SLE duration, systolic BP and diastolic BP), we used the Wilcoxon test to determine the CIs for the difference.
BP, blood pressure; HTN, hypertension; NSAIDs, non-steroidal anti-inflammatory drugs; SLE, systemic lupus erythematosus; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000.

recommended due to their additional beneficial effect in renal and cardiovascular disease.[16 17] The next most commonly used antihypertensive agent in our cohort, CCB, is useful in patients with Raynaud's syndrome and/or pulmonary artery HTN, important clinical manifestations of SLE.[16] Diuretics and beta-blockers have not been widely studied in hypertensive patients with SLE. While they can be efficacious, they may cause photosensitivity, a common comorbidity in SLE, with early reports suggesting they may trigger cutaneous lupus.[18] Beta-blockers may also worsen Raynaud's phenomenon, which is prevalent in SLE. Of note, many of our patients received combination HTN therapies.

Table 2 Logistic regression of patients with SLE treated for HTN: ORs for uncontrolled HTN (>130/80 mm Hg)

Variables	Unadjusted OR (95% CI)	Adjusted OR (95% CI)*
Male sex	1.00 (0.35 to 3.11)	1.27 (0.42 to 4.24)
Caucasian race/ethnicity	**2.33 (1.01 to 5.40)**	**2.72 (1.12 to 6.78)**
Age at last visit >65 years	1.69 (0.74 to 3.99)	1.68 (0.71 to 4.08)
Body mass index	1.06 (0.98 to 1.15)	**1.08 (1.00 to 1.19)**
SLE duration (years)	1.00 (0.97 to 1.03)	0.99 (0.96 to 1.02)
SLEDAI-2K ≥4	0.71 (0.32 to 1.60)	0.77 (0.33 to 1.76)
Renal damage ≥1	**0.36 (0.15 to 0.84)**	**0.39 (0.16 to 0.97)**
Using more >1 blood pressure medication	1.65 (0.71 to 4.08)	1.54 (0.63 to 3.96)
Prednisone	1.12 (0.37 to 3.81)	1.17 (0.38 to 4.14)
Non-steroidal anti-inflammatory drugs	2.06 (0.29 to 41.10)	1.99 (0.26 to 41.0)

Bolded values represent those that were statistically significant.
*Adjusted for: age at last visit, sex and race/ethnicity.
HTN, hypertension; SLE, systemic lupus erythematosus; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000.

In our cohort, Caucasians were more likely to have uncontrolled HTN. This finding differs from previous studies in SLE, which found that race/ethnicity groups traditionally at high risk of suboptimal BP control, such as African Americans, were indeed more likely to have resistant HTN.[5] However, Caucasian race has not always been associated with good HTN control in the general American population.[19] The observed associations between Caucasian race/ethnicity and uncontrolled HTN in our SLE sample may suggest that non-Caucasians were aggressively treated, perhaps because of the knowledge that this demographic is susceptible to poor outcomes. In addition, renal damage in our cohort was negatively associated with uncontrolled HTN (OR 0.39 95% CI 0.16 to 0.97), which is reassuring as controlling BP is key to preventing further renal damage. Although our analysis has adjusted for renal disease, this result may contribute to why Caucasian patients, with less renal damage than non-Caucasians, had poorer BP control. We noted that patients with higher BMI were more likely to have poor BP control (OR 1.08, 95% CI 1.00 to 1.19). Risk factors for uncontrolled HTN were analysed according to ACC/AHA guidelines, as they recommend a lower BP target, which could be beneficial to patients with SLE given the increased risk of cardiovascular disease. Of note, current published HTN guidelines do not specifically provide a target for patients with SLE, therefore studies aiming to define a target are needed. We could not draw definitive conclusions on the other variables assessed as the 95% CIs were imprecise and included the null value.

Potential limitations to our study should be noted. Our study was cross-sectional, and the BP of cohort patients was taken as a single measurement at annual visits. Further work using a longitudinal repeated measure design is needed to explore the effects of those variables, in addition to HTN treatment, disease activity, disease damage (eg, renal failure associated with SLE) and concomitant medications (eg, steroids, NSAIDs) on HTN in SLE. Also, we studied patients from a tertiary care centre within a specialised clinic, and within the setting of universal healthcare. The results do suggest that good BP control is possible in high-risk patients with SLE including non-Caucasians and those with renal damage, though this may be more difficult in other settings such as non-universal healthcare, where problems with healthcare access and patient adherence may create difficulties.

In summary, our cross-sectional analysis showed that 24.4% of patients with SLE were currently taking medications to treat HTN, and that over one-third required two or more medications concurrently. Angiotensin receptor blockers, ACEI and CCB were common antihypertensive choices, and diuretics were often used despite concerns in the literature regarding photosensitivity and lupus rash. Among the 108 patients taking antihypertensive medications, 39.8% had suboptimal control as per Canadian guidelines and 66.7% had suboptimal control as per ACC/AHA guidelines. In our cohort, Caucasian patients with SLE were more likely to have uncontrolled HTN, and we found a negative association between renal damage and our outcome. The results suggest that good BP control is possible in high-risk patients with SLE including non-Caucasians and those with renal damage, though this may be more difficult in other settings (such as non-universal healthcare and suboptimal care access).

Contributors JLL contributed to the design, interpretation of the data and writing of the manuscript. CAP, L-PG, EV and FK contributed to the collection of cohort data, design, interpretation of the data and writing of the manuscript. LL contributed to the design, analysis and interpretation of the data. SB contributed to the collection of cohort data, conception, design, interpretation of the data and writing of the manuscript. SB is the guarantor of this work, has full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors read and approved the final version of the manuscript.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

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