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BRIEF REPORT

Multidisciplinary Lupus Nephritis Clinic Reduces Time to Renal Biopsy and Improves Care Quality

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Objective. Patients with lupus nephritis (LN) have a 26-fold higher mortality rate compared with their peers. Kidney biopsy, the gold standard diagnostic method for LN, may have an average wait time of more than 50 days. Other gaps in quality process measures during LN visits have also been reported. A subspecialty multidisciplinary clinic (MDC) can provide better care and quality in LN; therefore, we aimed to examine how an LN MDC impacted time to biopsy, time to treatment, and other quality measures.

Methods. We included all validated patients with LN who underwent diagnostic kidney biopsies between the 2011 to 2017 pre-MDC period and the 2018 to 2020 post-MDC period. We compared time to biopsy and treatment and quality measures between the two periods and examined factors associated with timely LN diagnosis, defined as a biopsy within 21 days.

Results. During the pre- and post-MDC periods, 53 and 21 patients with LN underwent a diagnostic biopsy, respectively. We found a decrease in the median time to biopsy from 26 days to 16 days after starting the LN clinic ($P = 0.014$). Beyond clinical factors, the presence of social factors, such as being of a non-White race and having food insecurity, were associated with 54% lower odds of timely diagnosis (adjusted Hazards Ratio [aHR] = 0.46; 95% confidence interval: 0.22-0.93; $P = 0.031$). We found higher odds of quality measure performance during the post- versus pre-MDC period.

Conclusion. Wait times to diagnose LN decreased by 40% and higher quality measure performance was noted after establishing an LN MDC. Systemic and social barriers predicted delays in diagnosis that may be addressed by MDCs.

INTRODUCTION

Lupus nephritis (LN) contributes up to 10 times higher chronic kidney disease (CKD) progression, and patients with LN have a 10-fold higher risk of developing end-stage renal disease (ESRD) compared with age-matched peers (1). Notably, patients with LN have a 26-fold higher mortality rate compared with peers and lower 10-year survival compared with patients with systemic lupus erythematosus (SLE; or lupus) without nephritis (88% vs. 94%) (1). LN is a leading cause of ESRD, disability, and mortality in young women; thus, it is critical to diagnose LN in a timely manner to guide therapy to reduce CKD progression and mortality (2,3).

The 2012 American College of Rheumatology guidelines emphasizes the importance of renal biopsy as a gold-standard to diagnose and guide therapy in most patients with LN (4). Faurschou et al reported that a delay in diagnostic renal biopsy and starting therapy predicted 9-fold higher future ESRD risk (hazards ratio [HR] = 9.3, $P = 0.006$) (5). Such evidence emphasizes the critical need to reduce delays in diagnosing LN to reduce the risk of irreversible renal damage and improve survival (4,5). Additionally, using the Donabedian framework, access to care is a key quality process

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No potential conflicts of interest relevant to this article were reported.

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measure (6). Therefore, time to renal biopsy could be a critical indicator of LN care quality.

Our prior study highlighted that the average wait time to see a nephrologist and undergo a renal biopsy was over 50 days, with no change over two decades (1997-2017) (7). Other studies have shown that other high-impact quality measures, such as angiotensin-converting enzyme (ACE) inhibitor use and addressing social needs, were more often addressed in multidisciplinary clinics (MDCs) compared with general rheumatology clinics (8,9). Therefore, we implemented an LN MDC that included co-localized rheumatologists, nephrologists, social workers, pharmacists, and racially concordant nursing staff to provide targeted strategies to address barriers and improve care and outcomes. We aimed to examine time to biopsy and quality measures provided to patients with LN before and after the implementation of the LN MDC.

PATIENTS AND METHODS

Cohort

We identified all consecutive patients with clinical suspicion of LN who underwent a native renal biopsy to diagnose LN between January 1, 2011, and January 1, 2020, at the University of Wisconsin (UW) Hospital. Because the LN diagnostic and treatment guidelines significantly changed after 2011 (4), we only included patients with LN suspicion after 2011. We used standard classification criteria to validate LN diagnoses (10). The UW Institutional Review Board approved this study (IRB# 2016-1260). Patients who underwent kidney biopsy during a hospital admission were not included in our analysis.

We identified two periods: 1) the pre-MDC period included patients who underwent biopsies between January 1, 2011, and December 31, 2017, and 2) the post-MDC period included patients who underwent biopsies between January 1, 2018, and January 1, 2020.

Data

Socio-demographics and comorbidities. We used the electronic health record (EHR) and the comprehensive renal biopsy database to record patient, clinical, and biopsy characteristics. Hypertension (HTN) and diabetes mellitus (DM) were assessed using International Classification of Diseases Tenth Revision codes or problem list diagnoses. CKD stage was assessed using glomerular filtration rate at biopsy.

Renal histopathology. Renal biopsy was performed for clinical indications including edema, rising serum creatinine, hematuria, or proteinuria (4). Pathologic assessments of all biopsies were performed by renal pathologists according to the LN guidelines (10). Consistent with the 2003 International Society of Nephrology (ISN)/Renal Pathology Society (RPS) guidelines, we defined LN chronicity as the presence of any chronic lesions, which was uniformly reported in all LN biopsy reports, and examined the presence of LN chronic lesions in the two periods.

Primary outcomes: time to diagnostic renal biopsy and treatment. We determined the time from LN referral to diagnostic renal biopsy and the time from renal biopsy to treatment as our primary outcomes. To calculate the time to biopsy and LN therapy, we manually abstracted the following: 1) the first date of either initial abnormal labs raising suspicion of LN (persistent proteinuria >0.5 g per day plus hematuria or casts, persistent proteinuria >1 g per day, or increasing serum creatinine) (4) or the date of nephrology or rheumatology referral with suspicion of LN, 2) the date of LN biopsy, and 3) the date of the first LN specific therapy, excluding steroids.

Secondary outcome: Unmet social and pharmacy needs. We identified two key areas that could interrupt or delay LN care as unmet social barriers and issues with medication use, refills, or coverage (11). Quality process measures included assessing and addressing social needs and pharmacist consultation. We manually reviewed progress notes and referral orders to determine whether social issues were assessed or a social worker was requested (Supplementary Table 1 shows terms informed by the universal Social Determinants of Health, such as transportation and financial barriers and unstable housing, were searched to identify social needs) (12). We used similar methods to obtain data on whether pharmacy needs were assessed and addressed during both periods (Supplementary Table 1).

Tertiary outcome: guideline concordant therapeutic and preventive care. Previous studies have reported more than 20 quality measures covering specific aspects of lupus care to improve patient outcome, including preventive strategies (eg, vaccinations) and renal disease management (9,11). We collected data on the key quality measures from the EHR to determine the following rates.

1. Prophylactic vaccinations in both periods: We calculated vaccination rates within 1 year of LN diagnosis using EHR and state-wide immunization registry data by manually abstracting data on pneumococcal and influenza immunizations. To calculate pneumococcal vaccination rates, we included patients who received the 23-valent pneumococcal vaccine before the 2014 revision in the American College of Immunization & Prevention guidelines and those who received both 13-valent and 23-valent pneumococcal vaccinations after revision.

2. Preventive and therapeutic medication use: Based on the LN guidelines, we calculated medication use rates after LN diagnosis for three key medications: ACE-I/Angiotensin receptor blocker (ARBs), hydroxychloroquine, and hypoglycemic agents in patients with diabetes or hyperglycemia (4). We manually searched all charts to abstract medication use within 1 year of LN diagnosis.

Analysis

Descriptive data were expressed as the median for non-normally distributed data. Thus, median time to diagnosis was used to compare time to LN diagnosis during the two periods using Kaplan-Meier time-to-event analyses. Socio-demographics, therapy, LN chronicity, and quality measures were compared using Fisher's exact and *t*-tests. Predictors of timely LN diagnosis, defined as less than 21 days to LN biopsy, were examined using the Cox proportional hazards model. The European League Against Rheumatism LN guidelines recommend obtaining an early kidney biopsy to confirm LN diagnosis (13). Previous studies used 3- to 6-month cutoffs to define timely LN biopsy and diagnosis, which can lead to significant delays in starting steroid-sparing LN therapy (2,3) Consistent with the US Department of Defense (DoD) recommendations for access to care, we used 2 weeks (<15 days) to define time to nephrology evaluation (14,15), and assuming a 1-week procedural scheduling lag, we used a cutoff of 21 days to define timely LN diagnosis. We included the presence of social factor(s), pre- and post-MDC periods, age, sex, and CKD stage of 3 or more at LN diagnosis in our analysis based on the published literature (16). Social factors included non-White race and/or the presence of social barriers such as lack of transportation, unstable housing, and food insecurity. For the purpose of analysis, we categorized social factors as "no social factors noted" or "one or more social factors noted." We reviewed EHRs to identify the underlying causes leading to delays in LN diagnosis. R version 3.4.1 was used for all analyses.

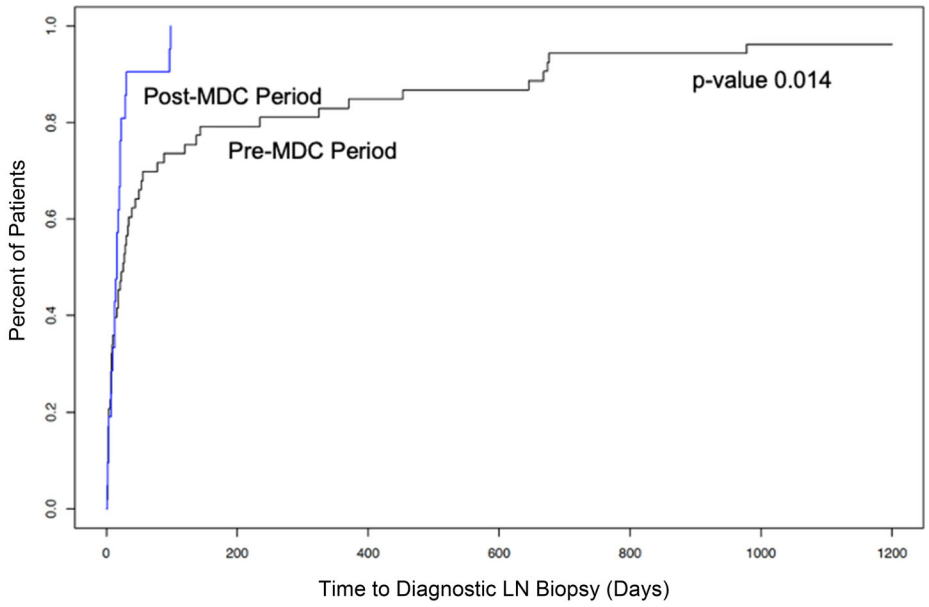
RESULTS

In the pre-MDC period, the mean age was 36 ± 14 years, 75% were female, and 74% were White (Table 1). Social barriers were noted in 9% of the patients. In the post-MDC period, the mean age was 35.6 ± 13 years, 62% were women, and 52%

Table 1. Characteristics of adult LN patients who underwent diagnostic kidney biopsy

	Pre-MDC n = 53	Post-MDC n = 21	OR (95% CI)[a]	*P* value[b]
Socio-demographics				
Age, mean ± SD, y	36 ± 14	35.6 ± 13	–	0.91
Female	40 (75%)	13 (62%)	0.5 (0.2-1.8)	0.26
White race	39 (74%)	11 (52%)	–	–
Non-White race	14 (26%)	10 (48%)	2.5 (0.8-8.2)	0.10
Social barriers noted	**5 (9%)**	**12 (57%)**	**12.0 (3.1-56)**	**<0.0001**
Smoking ever	20 (38%)	6 (29%)	0.6 (0.2-2.1)	0.43
CKD stage ≥3	17 (32%)	10 (48%)	1.7 (0.5-5.5)	0.42
Time to LN biopsy				
Mean ± SD, d	**202 ± 489**	**22 ± 26**	–	**0.0103**
Median (IQR), d	**26 (7-120)**	**16 (8-21)**	–	**0.014**
Time to LN therapy				
Median (IQR), d	7 (1-16)	7 (3-12)	–	0.204
LN therapy started				
MMF	35 (66%)	18 (86%)	3 (0.7-18)	0.15
CYC	9 (17%)	0	0 (0-1.2)	0.053
Others (RTX, tacrolimus)	**2 (4%)**	**5 (24%)**	**7.7 (1.1-88)**	**0.017**
HCQ use	41 (77%)	20 (95%)	5.8 (0.8-262)	0.09
LN chronicity, present	30 (56%)	13 (61%)	0.9 (0.4-2.3)	0.85
Access to social and other services				
Social work consultation	**4 (8%)**	**11 (52%)**	**15 (4-81)**	**<0.0001**
Pharmacist consultation	0	7 (33%)	–	<0.0001
Preventive and therapeutic care				
ACE-I/ARB present	**32 (60%)**	**20 (95%)**	**13 (1.8-567)**	**0.008**
DM and started therapy	2 (4%)	4 (19%)	5.4 (0.7-65)	0.06
Flu vaccination	43 (81%)	18 (85%)	1.3 (0.03-8.0)	0.99
Pneumococcal vaccination	**19 (36%)**	**18 (86%)**	**10 (2.6-62)**	**0.0002**

Note: Significant values are in bold.
Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; AZA, azathioprine; CI, confidence interval; CKD, chronic kidney disease; CYC, cyclophosphamide; DM, diabetes mellitus; Dx, diagnosis; HCQ, hydroxychloroquine; IQR, interquartile range; LN, lupus nephritis; MDC, multidisciplinary clinic; MMF, mycophenolate; OR, odds ratio; RTX, rituximab.
[a]OR calculated using Fisher's test for qualitative data and *t*-test for quantitative data.
[b]*P* value calculated using Fisher's test for qualitative data and *t*-test for quantitative data.



Number At Risk:

Time (Days)	0	22-60	61-120	121-300	301-600	601-900	>900
Pre-MDC	53	28	16	13	10	7	3
Post-MDC	21	5	2	0	0	0	0

Figure 1. Kaplan Meier plot showing time to outpatient diagnostic lupus nephritis (LN) biopsy during pre- (2011-2017) and post- (2018-2020) multidisciplinary clinic (MDC) periods including all patients.

were White (vs. 74% in pre-MDC period, $P = 0.10$, Table 1). Social barriers were noted in 57% of the patients. We noted 38% more social barriers being identified during the post-MDC period compared with the pre-MDC period (57% vs. 9%, $P < 0.0001$; Table 1). No difference was noted between the presence of LN chronic lesions in the two periods (56% vs. 61%, $P = 0.85$).

MDC reduced time to diagnostic renal biopsy. The median time to biopsy in the pre-MDC period was 26 days (interquartile range 7-120), compared with 16 days (interquartile range 8-21) in the post-MDC period. The time to biopsy was significantly lower in the post-MDC period compared with the pre-MDC period including all patients ($P = 0.014$, Figure 1). The mean time to LN biopsy decreased from 202 days to 22 days in the post-MDC period ($P = 0.01$, Table 1).

No change in time to LN therapy in both pre- and post-MDC periods. We found no difference in the median time to therapy ($P = 0.20$) between the two periods. A higher use of

Table 2. Predictors of timely LN diagnosis (within 21 days including time to nephrology evaluation followed by kidney biopsy)

Variable	HR (95% CI)	*P* value	aHR (95% CI)	*P* value
Age at LN biopsy ↑ 10 y	0.98 (0.96-1.01)	0.13	**0.97 (0.94-1.0)**	**0.012**
Male	Ref	Ref	Ref	Ref
Female	0.89 (0.48-1.7)	0.74	0.85 (0.42-1.7)	0.65
No social factors noted	Ref	Ref	Ref	Ref
≥1 social factors noted	0.81 (0.45-1.4)	0.46	**0.46 (0.22-0.93)**	**0.031**
CKD stage <3	Ref	Ref	Ref	ref
CKD stage 3 or above	1.1 (0.62-2.1)	0.69	1.6 (0.79-3.3)	0.19
Pre-MDC period	Ref	Ref	Ref	Ref
Post-MDC period	1.7 (0.92-3.2)	0.09*	**2.2 (1.1-4.4)**	**0.026**

Note: Multivariable model includes all variables: age, social factors (including racial group and/or the presence of social barriers such as lack of transportation or financial assistance, food insecurity, or housing insecurity), sex, CKD stage ≥3, and pre- and post-MDC periods.
Abbreviations: aHR, adjusted hazards ratio; CI, confidence interval; CKD, chronic kidney disease; HR, hazards ratio; LN, lupus nephritis; MDC, multidisciplinary clinic; Ref, reference.
*$p < 0.1$, trend of significance.

other immunosuppressive therapies (rituximab, tacrolimus) was noted during the post-MDC period (odds ratio [OR] 7.7, Table 1).

Improved access to social services and preventive care in post-MDC period. We found higher quality measures performance during the post-MDC period. We found 15-fold higher odds of assessment and addressing social needs during the post-MDC period (OR 15, $P < 0.0001$) (Table 1). We noted higher pharmacist consultation rate in the post-MDC period ($P < 0.0001$) compared with no consultation offered during the pre-MDC period. Furthermore, patients seen in the MDC had 10-fold higher odds to receive pneumococcal vaccination (OR 10, $P = 0.0002$; Table 1) and 13-fold higher odds to be started on ACE inhibitors (OR 13, $P = 0.008$).

Risk factors for delayed LN diagnosis. The presence of one or more social factors— such as food insecurity, transportation and financial barriers, unstable housing, and stress—were associated with 54% lower risk of timely LN diagnosis (adjusted HR 0.46, $P = 0.031$; Table 2). Furthermore, we noted that patients seen in an MDC had a 2.2-fold higher risk of receiving a timely LN diagnosis (HR = 2.2, $P = 0.026$, Table 2). We noted that 90% of the delays occurred because of delays in scheduling appointments with specialists, cancellations due to outstanding medical bills or homelessness, or no-shows for appointments due to lack of transportation, whereas 10% of the biopsy appointments were rescheduled because of uncontrolled blood pressure, abnormal labs, or per provider decision. In the post-MDC period, a social worker and a pharmacist closely followed patients after visits to address such barriers.

DISCUSSION

In summary, our study reported a significant reduction in wait times to diagnose LN and higher quality measure performance after establishing an LN MDC. We report changes in time to LN biopsy after implementing an LN MDC. We also found that social factors (including non-White race) and the presence of social barriers (such as food insecurity and unstable housing) could predict delays in LN diagnosis that can be addressed by including a social worker in SLE clinics.

Lupus is associated with a 10-fold higher risk of ESRD (17). Despite the availability of new LN therapies, mortality due to LN in the United States increased from 2015 to 2019 (18), which could reflect delays in diagnosis or interrupted care due to social barriers. Studies have shown that patients with lupus without insurance or with public insurance (Medicaid) have lower LN screening rates and higher loss to follow-up contributing to ESRD risk (19). Finally, we previously reported prolonged wait times for renal biopsy in patients with LN over 20 years (1997-2017), with a median delay of 52 days from the time of nephrology referral (7). Such prolonged wait times represent a barrier to providing efficient care in LN.

MDCs help coordinate complex management and deliver patient-centered care by providing access to relevant specialists co-located at a single site. For example, the SLE MDC at Rush University reported improvement in overall quality of care in lupus (9). Arora et al reported better performance on 20 SLE care quality measures in patients managed in the MDC versus general rheumatology clinics (8,9). Furthermore, Yazdany et al reported that better performance on process measures in clinical settings and patients receiving higher care quality were significantly protective against accrued lupus damage (adjusted OR 0.4; 95% confidence interval: 0.4-0.7). Additionally, social support and coping are modifiable factors that affect patient satisfaction with care and promote retention in care (9). Such factors could be addressed by a collaborative, MDC model including a social worker and racially concordant staff (20).

Our LN MDC at UW-Madison includes a co-localized rheumatologist, nephrologist, pharmacist, social worker, and dedicated nursing and medical assistant staff. In this study, we identified that non-White race and the presence of social barriers independently determined delays in LN diagnosis. After implementation of our LN MDC, we were able to address such delays and improve care quality with the help of social services, pharmacists, racially concordant staff, rheumatologists, and nephrologists co-located in our clinic. We noted a clear improvement in both mean and median time to biopsy in the post-MDC period. However, the variability in patient presentations, social barriers leading to delays, and care patterns make an evaluation of the process measure for access to care challenging. We noted that the median time to specific therapy was not different between the two periods. However, the time from clinical suspicion of LN to implementing steroid-sparing therapy was significantly affected owing to the delay in LN biopsy. At our institution, patients often first see a nephrologist for a clinical evaluation followed by a kidney biopsy. Thus, co-locating nephrologists and rheumatologists at our LN MDC reduced wait times to see specialists and prompted timely biopsy and initiation of LN therapy. Other strategies, including early involvement of nephrology and interventional radiology for patients with suspicion of LN, can prompt a timely LN diagnosis and the initiation of LN therapy. Moreover, targeting social barriers that can interrupt care by including a social worker in the clinic could help reduce delays in diagnosis. Similar to previous studies, we found that, after implementing an LN MDC, we were able to initiate timely prevention in patients with LN (9). For instance, we reported 10-fold higher pneumococcal vaccination rate in our LN MDC.

Despite the strengths of this study, such as the inclusion of a biopsy-proven incident LN cohort, manual validation for all quality measures, and meeting 18 out of 18 Squire checklist items, we also acknowledge limitations. First, institutional policies are not universal, and nephrologists might not perform biopsies in other

institutions. Thus, early involvement of nephrology and interventional radiology for patients with suspicion of LN could help reduce delays in diagnosis at other institutions. Second, the National Institutes of Health (NIH) LN chronicity index was not uniformly reported in the pre-MDC period, which could explain why we found no difference in the burden of LN chronicity in the two periods. Third, our sample size was small, and 81% of the patients were White, which limits the generalizability of our findings. Additionally, we used an exploratory cutoff of 21 days to define timely diagnosis based on the DoD benchmarks and welcome data regarding other time quality definitions (14,15). Finally, comorbidities like HTN and DM were not manually validated.

In conclusion, after implementing the LN MDC at our institution, we noted a significant reduction in wait time to diagnose LN and higher quality of care. We noted that by including a social worker and racially concordant staff, we were able to address social barriers leading to delays in diagnosis. Our MDC provides consistent care to monitor response to therapy (and change therapy if lack of response potentially sooner), and we provide ancillary care of social work and pharmacy to target barriers that interrupt care. Additionally, our MDC provides prompt evaluation and initiation of therapy, which may improve LN outcomes over time. Improvement in LN outcomes over time in the post-MDC period will be assessed in future studies.

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AUTHOR CONTRIBUTIONS

Dr. Garg drafted the article, and all authors revised it critically for important intellectual content. All authors approved the final version to be published. Drs. Garg, Panzer, and Singh had full access to all of the data in the study and take responsibility for the accuracy of the analysis.
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