Use of telemedicine for follow-up of lupus nephritis in the COVID-19 outbreak: The 6-month results of a randomized controlled trial

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Abstract

Objective: This study aimed to evaluate the short-term patient satisfaction, compliance, disease control, and infection risk of telemedicine (TM) compared with standard in-person follow-up (FU) for patients with lupus nephritis (LN) during the COVID-19 pandemic.

Method: This was a single-center open-label randomized controlled study. Consecutive patients followed at the LN clinic were randomized to either TM or standard FU (SF) group in a 1:1 ratio. Patients in the TM group received FU via videoconferencing. SF group patients continued conventional in-person outpatient care. The 6-month data were compared and presented.

Results: From June to December 2020, 122 patients were randomized (TM: 60, SF: 62) and had at least 2 FUs. There were no baseline differences, including SLEDAI-2k and proportion of patients in lupus low disease activity state (LLDAS), between the two groups except a higher physician global assessment score (PGA) in the TM group. After a mean FU of 19.8 ± 4.5 weeks, the overall patient satisfaction score was higher in the TM group. More patients in the TM group had hospitalization (15/60, 25.0% vs 7/62, 11.3%; p = .049) with higher baseline PGA (OR = 1.17; 95% CI, 1.08–1.26) being the independent predictor. The proportions of patients remained in LLDAS were similar in the two groups (TM: 75.0% vs SF: 74.2%, p = .919). None of the patients had COVID-19.

Conclusions: TM FU resulted in better patient satisfaction and similar short-term disease control in patients with LN compared to standard care. However, it was associated with more hospitalizations and might need to be complemented by in-person visits especially in patients with higher PGA.

Keywords

COVID-19, lupus nephritis, systemic lupus erythematosus, telehealth, telemedicine

Introduction

Patients with systemic lupus erythematosus (SLE) are at increased risk of severe COVID-19 due to the underlying disease, comorbidities and use of immunosuppressants (IS).[1,2] During the pandemic, vulnerable patients such as those with lupus nephritis (LN) face the difficult choice between COVID-19 infection risk during a clinic visit and postponing the needed care. Many patients had a high level of anxiety regarding their risk of mortality from the infection and supported lockdown/shielding at least in the initial phase of the outbreak.[3] Diversion of resources to COVID-19 might also contribute to adverse physical and mental outcomes of the patients.[4] An alternative option

would be to adopt telemedicine (TM) or telehealth, the use of telecommunication technologies to provide medical information and services, to maintain medical care while minimizing exposure. Indeed, the use of TM has been recommended by international rheumatology societies after the outbreak.[5,6] Various modes of delivery of TM, including

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synchronous (i.e., video and telephone) and non-synchronous (i.e., email and short message service), are available, with video consultation more advocated.[7]

Despite being widely adopted during this pandemic, the evidence supporting the use of TM in rheumatology has been limited. According to a systematic review in 2017, there is no good evidence in supporting the use of TM for managing rheumatic diseases due to the high risk of bias of the published studies.[8] In a subsequent randomized controlled trial (RCT), it was concluded that a TM follow-up (FU) could achieve similar disease control as conventional care in rheumatoid arthritis patients with low disease activity or remission.[9] Two studies conducted during the COVID-19 outbreak reported moderate acceptance of TM as the mode of care in patients with connective tissue diseases, which might be influenced by the subjective disease activity and some socio-economic factors.[10–12] However, there is no data on the outcome of TM FU in patients with LN. We hypothesize that TM is a feasible and safe mode of health-care delivery while maintaining disease control in these patients.

We conducted a RCT comparing TM and standard in-person FU for patients with LN. In view of the need for timely evidence on this novel mode of care, we reported the 6-month results of the study focusing on patient satisfaction, compliance, disease control, and infection risk during the COVID-19 outbreak.

Methods

Study design and patients

This was a single-center open-label RCT conducted at a regional hospital in Hong Kong. From May 2020, consecutive adult patients with a diagnosis of SLE according to the 2019 EULAR/ACR classification criteria followed up at the LN clinic were invited to participate in the study.[13] Patients (or carers) needed to possess the technology for conducting a TM visit (a smartphone, tablet, or computer with audio and video capabilities and internet connection). Patients were excluded if they were pregnant or incapable of answering a questionnaire. Participants were randomized 1:1 to either TM (TM group) or standard FU (SF group) using a computer-generated random number sequence. They were asked to fill in an online questionnaire post-consultation regarding their satisfaction of various aspects of the FU (supplementary figure 1). The responses were assigned a value of 0–4 (strongly disagree to strongly agree), with a higher score indicating that the respondent was satisfied with the FU and a two indicating a neutral response.

Interventions and assessments

Patients randomized to receive TM FU were scheduled for a real-time face-to-face video consultation via a commercial video teleconference software ZOOM (Zoom Video Communications Inc, California, US). Patients in the SF group received standard in-person outpatient care. An in-person clinic consultation could be arranged as required by the patients or clinicians. Similarly, a TM consultation could be arranged as required. The frequency of visits was based on clinical judgments, as well as joint decisions of the attending rheumatologists and patients.

Disease-related variables recorded at baseline included disease duration, comorbidities, LN class, 24-h urine protein, IS use, SLE disease activity, and SLICC/ACR Damage Index (SDI).[14] Prior to each consultation the patients needed to have blood and 24-h urine total protein checked. SLE disease activity at each consultation was assessed by SLEDAI-2k and physician global assessment (PGA).[15] Disease flares were captured with the SELENA flare index.

Recently, remission and lupus low disease activity state (LLDAS) were agreed to be the meaningful targets for managing lupus patients in order to prevent damage accrual and improve quality of life.[16] In both groups, medication titration was aiming at achieving remission or LLDAS. All FUs were performed by rheumatologists or nephrologists with more than 3 years of experience in managing patients with LN.

Statistical analysis

The patients in the TM and SF groups were compared by chi-squared test or Fisher's exact test and Student's t-test or Mann-Whitney U test where appropriate, at baseline and at the latest FU. Differences in the changes from baseline to the latest FU within-group (e.g., disease activity parameters) were analyzed by Wilcoxon test, and between-group changes by Mann-Whitney U test. Multivariate regression models were used to adjust for the baseline differences between the two groups if any. A 2-tailed probability value of $p < 0.05$ was considered statistically significant. Statistical analyses were performed using the SPSS (V.26.0, IBM Corporation, Armonk, NY, USA).

Results

From June to December 2020, 122 patients were randomized (TM: 60, SF: 62) and had at least two FUs (Figure 1). At baseline, the mean age of the patients was 44.4 ± 11.5 years with a mean disease duration of 15.1 ± 9.0 years. Almost all patients had biopsy-proven LN class III, IV, or V (88.5%) and were on prednisolone (91.8%). The majority of them (73.8%) were on IS with the commonest being mycophenolate mofetil (47.5%). While 63.9% of the patients were in LLDAS, none achieved disease remission. There were no baseline differences between the two groups except a higher PGA was observed in the TM group (mean, 0.67 ± 0.69 vs 0.45 ± 0.60, $p = .003$) (Table 1).
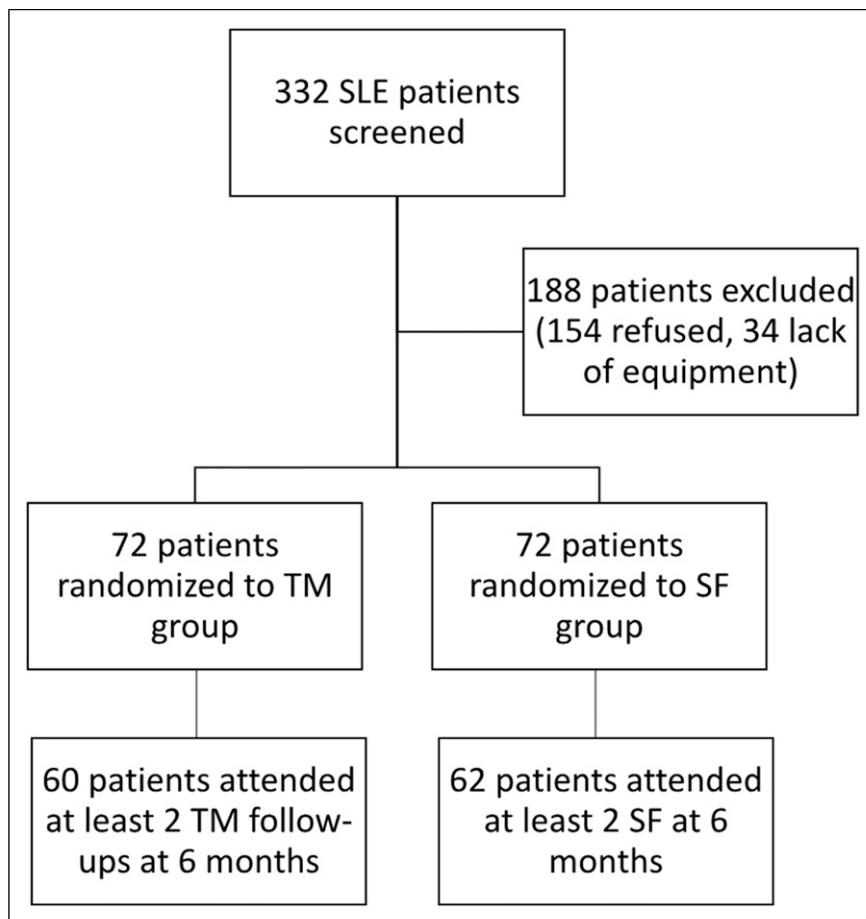
Figure 1. Trial profile. TM = telemedicine, SF = standard follow-up.

The mean FU duration was 19.8 ± 4.5 weeks. There were, in total, 371 visits (TM: 184, SF: 187). When comparing the most recent visit, the mean waiting time from entering the clinic waiting room (virtual or real) to seeing a doctor was significantly shorter in the TM group (22.5 ± 28.6 min vs 68.9 ± 40.7 min, $p < .001$) (Figure 2(a)). The mean overall patient satisfaction score was higher in the TM group (2.2 ± 0.6 vs 1.9 ± 0.8, $p = .042$). The patients' satisfaction was similar in terms of the consultation alone (TM: 2.2 ± 0.6 vs SF: 2.1 ± 0.8, $p = .251$) as well as the explanation for medication usage and side effects (TM: 2.1 ± 0.8 vs SF: 2.1 ± 0.7, $p = .596$). Age was not found to be associated with patient satisfaction. The results of the post-consultation satisfaction questionnaire are shown in detail in Figure 2(b).

The mean number of visits was similar in the two groups (TM: 3.1 ± 1.3 vs SF: 3.0 ± 1.2, $p = .981$). However, there was a trend suggesting that alternative mode of FU was being requested more frequently in the TM group than the SF group (TM: 12/60, 20.0% and SF: 5/62, 8.1%; $p = .057$). The main reasons in the TM group were perceived flares or new symptoms, while that for the SF group was fear of

contracting SARS-CoV-2 (supplementary table 1). More patients in the TM group had hospitalization (15/60, 25.0% vs 7/62, 11.3%; $p = .049$) within the study period. Logistic regression analysis revealed baseline PGA (OR = 1.17, 95% CI, 1.08–1.26, $p < .001$) rather than TM FU (OR = 0.499, 95% CI, 0.163–1.52, $p = .222$) was significantly associated with hospitalization after controlling for age and gender. Hospitalizations related to SLE was numerically higher in the TM group (TM: 9/60, 15.0% and SF: 4/62, 6.5%; $p = .151$) (supplementary table 2). None of the patients had COVID-19 and there was no mortality in either group during the study period.

The proportions of patients remained in LLDAS were similar in the two groups (TM: 75.0% vs SF: 74.2%, $p = .919$) (supplementary figure 2). The within-group changes were not significant (TM: $p = .064$; SF: $p = .804$). Although the PGA was still higher in the TM group (0.52 ± 0.49 vs 0.36 ± 0.40, $p = .025$), there was no difference in the SLEDAI-2k between the two groups (TM: 3.6 ± 1.9 vs SF: 3.5 ± 2.5, $p = .655$). The within-group and between-group changes in PGA over time were also not significant. At the last visit, there was no difference in the mean 24-h

Table 1. Baseline clinical data of the recruited patients and comparison between the telemedicine/standard follow-up groups.

	Overall (n = 122)	Telemedicine group (n = 60)	Standard follow-up group (n = 62)	p-value
Age in years	44.4 ± 11.5	44.1 ± 11.7	44.7 ± 11.5	0.779
Gender: Female	111 (91.0)	55 (91.7)	56 (90.3)	0.796
Disease duration in years	15.1 ± 9.0	16.2 ± 8.7	14.0 ± 9.1	0.115
Nephritis class III, IV, or V	108 (88.5)	54 (90.0)	54 (87.1)	0.427
24-h urine proteinuria in gram	0.51 ± 0.63	0.53 ± 0.60	0.50 ± 0.65	0.712
Current use of prednisolone	112 (91.8)	57 (95.0)	55 (88.7)	0.323
Daily prednisolone dose in mg	5.51 ± 4.21	5.69 ± 4.17	5.34 ± 4.29	0.570
Use of immunosuppressant	90 (73.8)	46 (76.7)	44 (71.0)	0.474
SLEDAI-2K	3.7 ± 2.3	4.0 ± 2.3	3.3 ± 2.3	0.097
PGA	0.56 ± 0.65	0.67 ± 0.69	0.45 ± 0.60	**0.003**
LLDAS	78 (63.9)	36 (60.0)	42 (67.7)	0.251
Remission	0 (0)	0 (0)	0 (0)	nn/a
Presence of comorbidity	87 (71.3)	40 (66.7)	47 (75.8)	0.264
Number of comorbidity	1.3 ± 1.3	1.5 ± 1.5	1.2 ± 1.1	0.866
SDI	0.9 ± 1.2	1.1 ± 1.3	0.8 ± 1.0	0.243
HAQ-DI	0.23 ±0.46	0.25 ± 0.47	0.21 ± 0.44	0.571
HADS				
Anxiety scale	6.1 ± 4.1	6.2 ± 4.2	5.9 ± 4.1	0.720
Depression scale	5.7 ± 4.3	5.7 ± 3.9	5.7 ± 4.7	0.724
Lupus QoL score for				
Physical health	79.1 ± 20.3	78.2 ± 20.3	80.1 ± 20.3	0.534
Pain	81.3 ± 19.3	81.4 ± 19.2	81.2 ± 23.0	0.230
Planning	83.5 ± 18.1	83.2 ± 16.1	83.7 ± 20.0	0.533
Intimate relationship	74.2 ± 27.7	72.4 ± 28.5	75.6 ± 27.3	0.578
Burden to others	74.2 ± 23.2	72.9± 20.9	75.5 ± 25.3	0.153
Emotional health	80.5 ± 18.1	79.9± 16.6	81.0 ± 19.6	0.487
Body image	77.0 ± 24.1	77.3± 20.2	76.6 ± 27.5	0.428
Fatigue	73.7 ± 20.4	73.2± 19.8	74.1 ± 21.0	0.665

Data are reported as mean ± SD or number (%). SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index 2000; PGA: physician global assessment; LLDAS: lupus low disease activity state; SDI: Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index; HAQ-DI: Health Assessment Questionnaire Disability Index; and HADS: Hospital Anxiety and Depression Scale.

proteinuria (TM: 0.52 ± 0.63 g vs SF: 0.54 ± 0.73 g, p = .894) and prednisolone daily dose (TM: 6.04 ± 5.09 mg vs SF: 4.63 ± 2.68 mg, p = .073) between the two groups.

Discussion

As we define the new normal in the COVID-19 era, we need a new approach to provide care for our LN patients, and TM has been the widely used alternative despite the lack of evidence. This is the first clinical trial comparing TM versus standard in-person FU for LN. We found that the overall patient satisfaction was higher in the TM group which could be partially driven by the shorter pre-consultation waiting time. On the other hand, this might also be related to the intrinsic logistic convenience of TM, for example, time saved from traveling. TM-based care appeared to be well received by patients with rheumatic diseases during the pandemic. In a Spanish study, it was found that for general rheumatic diseases, the transfer of care to tele-conferencing was met with a considerable degree of satisfaction for both patients and doctors.[17] In another recent study in rheumatic patients with predominantly rheumatoid arthritis, 71.2% were satisfied with their virtual appointment.[18]

The early results of our study showed that the proportions of patients remained in LLDAS were similar in both groups suggesting TM could be a valid option for LN FU. A unique and fundamental element of disease activity assessment in LN is the monitoring of proteinuria. This renders a virtual FU potentially more attractive for LN than other rheumatic diseases where a physical examination is more essential. To this end, the development and validation of patient-reported outcomes are encouraged. An observational study done during the pandemic also showed the disease activity at the next visit and the corticosteroid dosages prescribed were similar between teleconsultations and physical FUs in SLE patients.[19] Due to the low incidence of COVID-19 in Hong Kong, whether TM FU could reduce the infection risk could not be properly tested.
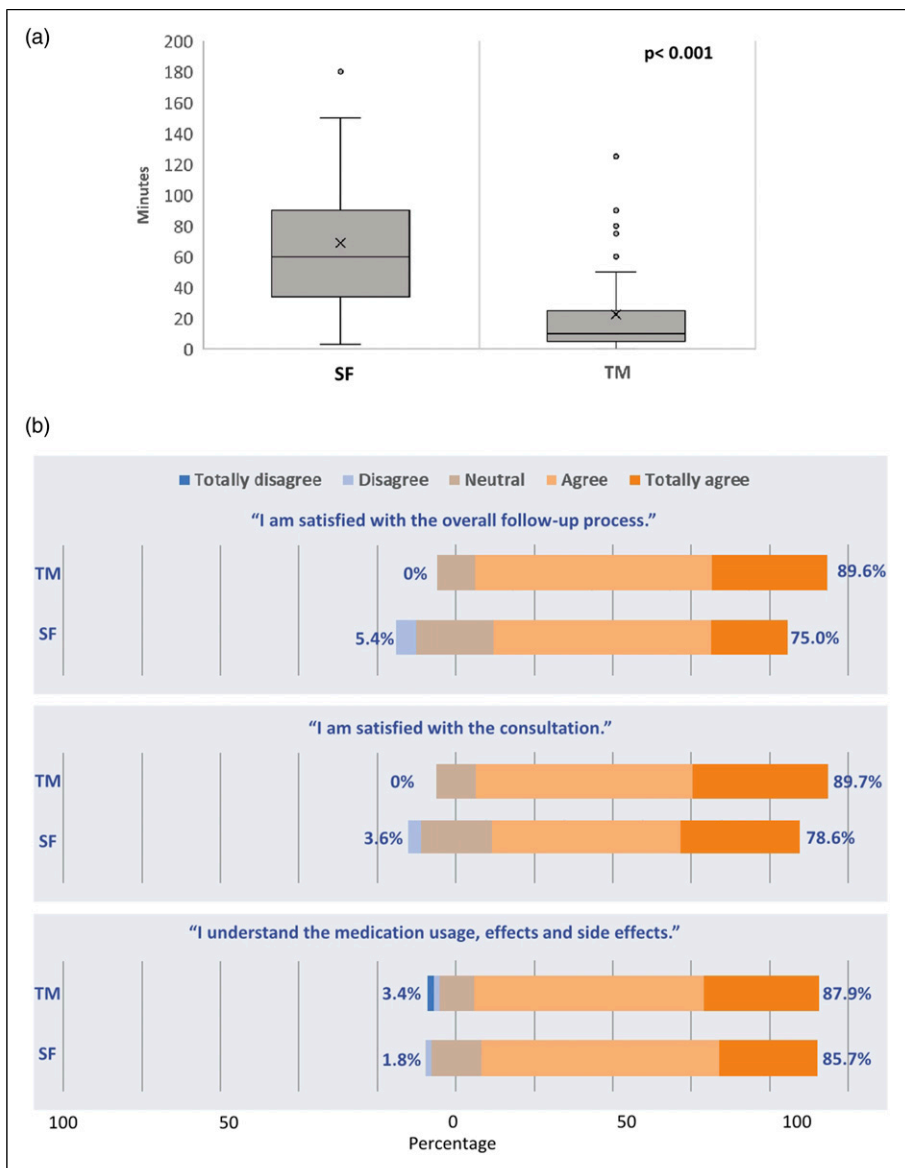
Figure 2. (a) Waiting time between entering the clinic waiting room (virtual or real) and seeing a rheumatologist. TM = telemedicine and SF = standard follow-up. (b) The results of the post-consultation satisfaction questionnaire. Response is shown as percentage with positive responses on the right. The neutral category was removed when calculating percentages.

In this study, patients in the TM group had more hospitalizations and a higher tendency to change to SF than the reverse. These could off-set the conceived advantages of TM. Although the patients in the TM group had higher baseline PGA which confounded the results, there was no significant difference in the objective measures of lupus disease activity. In fact, the PGA in the TM group was persistently higher compared to that of the SF group which could be explained by the perceived higher disease activity when the assessment was done virtually. The increased hospitalizations might reflect the lack of confidence of either patients or clinicians in accurately assessing the clinical condition. In fact, a recent study revealed that 93% of the surveyed clinicians and 86% of the patients with autoimmune rheumatic diseases (32% with SLE) rated TM as worse than physical consultations in terms of assessment accuracy.[20] It appeared that patients with higher physician-assessed disease activity might not be optimally managed by TM alone. A hybrid mode of FU with TM complemented by in-person visits when necessary might be helpful.

There are several limitations. First, it was impossible to blind the patients and clinicians, the possibility of bias could not be eliminated. Second, only the 6-month results of the study were presented. The long-term efficacy and

cost-effectiveness results will be available when the 1-year FU has been completed. Moreover, a comprehensive analysis of use of TM should be based on a relevant conceptual framework, such as the technology acceptance model.[21] Third, selection bias could occur as only patients who preferred TM were enrolled, although we found no difference in the baseline clinical characteristics between the participants of the study and those who refused TM (data not shown). Lastly, our results should be interpreted in the context of the local COVID-19 transmission rate and anti-endemic measures which could affect the acceptance of TM.

Conclusion

We reported the early results of the first RCT comparing TM and standard FU in patients with LN. During the COVID-19 outbreak, TM FU resulted in better overall patient satisfaction. However, it was associated with more hospitalizations. The preliminary data suggested TM was equally efficacious in maintaining disease control in patients with LN in short-term, although it might need to be supplemented by in-person visits, especially in patients with higher physician assessed disease activity.

Contributors

All authors critically revised the manuscript for important intellectual content. Specific roles included study design (HS, CCS, and LST), data collection (HS, EC, ITC, SLL, and TKL), data analysis (HS, EC, ITC, SLL, and TKL), and drafting of manuscript (HS and LST).

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Patient and public involvement

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

Patient consent for publication

Written informed consents were obtained from all patients.

Ethical approval information

The Joint Chinese University of Hong Kong – New Territories East Cluster Clinical Research Ethics Committee, No. 2020-0254

Data sharing statement

Data can be shared upon request.

Supplemental Material

Supplemental material for this article is available online.

Notes

1. Trial registration number NCT04368299

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