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Novel Indices for Lumbar Discectomy: Systemic Immune Inflammation Index, Systemic Inflammatory Response Index, Multi Inflammatory Index, and Prognostic Nutrition Index

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ABSTRACT

AIM: To evaluate systemic immune inflammation index (SII), systemic inflammatory response index (SIRI), multi-inflammatory index (MII), and prognostic nutrition index (PNI), and to compare them with the previously reported inflammation-related hematologic index in lumbar discectomy (LD).

MATERIAL and METHODS: This was a retrospective, cross-sectional, single-center study with 105 consecutive patients who underwent surgery for LD. The study comprised three groups: Group I included data from healthy participants, Group II included data before LD, and Group III included data after LD. We analyzed mean platelet volume (MPV), platelet–lymphocyte ratio (PLR), neutrophil–lymphocyte ratio (NLR), SIRI, SII, MII, and PNI, in comparison with the Roland–Morris Disability Questionnaire (RMDQ), Oswestry Disability Index (ODI), and Visual analog scale for leg (VASLeg).

RESULTS: CRP and MPV were similar for the preoperative and postoperative periods (p=0.489). In the postoperative measurements, NLR, PLR, SII, and SIRI increased (p<0.0001). On the contrary, PNI decreased with LD (p<0.0001). NLR (p<0.001), SII (p<0.001), and SIRI (p<0.001) were the valuable indices for LD. PLR (p<0.001), MII-1 (p=0.004), and MII-2 (p<0.001) also predicted LD. ODI, RMDQ, and VASLeg correlated with MII-1, MII-2, and SIRI.

CONCLUSION: LD's most substantial and valuable indices were NLR, SII, and SIRI. Regarding superiority to SII and NLR, SIRI showed significant agreement with the scales and drew a more appropriate marker profile for LD than MII-1, MII-2, and PNI.

KEYWORDS: Lumbar discectomy, Systemic immune inflammation index, Systemic inflammatory response index, Multi inflammatory index, Prognostic nutrition index

ABBREVIATIONS: ODI: Oswestry Disability Index, **PI:** Pelvic Incidence; **PT:** Pelvic Tilt; **SS:** Sacral Slope, **RMDQ:** Roland–Morris Disability Questionnaire, **VASLeg:** Visual analog scale for leg, **WD:** Walking Distance, **MII:** Multi Inflammatory Index, **NLR:** Neutrophil-to-lymphocyte ratio, **PLR:** Platelet-to-lymphocyte ratio, **SII:** Systemic immune inflammation index, **SIRI:** Systemic inflammatory response index, **PNI:** Prognostic nutrition index, **MPV:** Mean Platelet Volume, **AUC:** Area Under the Curve, **SE:** Standard error, **CI:** Confidence Interval.

INTRODUCTION

A herniated lumbar disc is a condition that develops when a tear occurs at the edges of the disc joint between the vertebrae, and the contents of the disc enter the spinal canal, compressing the nerves going to the legs, and sometimes on the spinal cord (21). By forcing the disc, pressure is mounted on the nerves coming out of the spinal cord, which can cause severe pain. Recent studies have shown that the resulting state of inflammation leads to both

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pain and poor postoperative recovery (10). Physiotherapeutic applications can reduce herniated disc pain, inflammation, and muscle spasm. However, when they are insufficient, lumbar discectomy (LD) is the most common surgical procedure for patients with low back pain and leg symptoms (1,17).

Increased inflammatory states strongly influence the efficacy of surgical interventions and the post-surgical healing process in the affected spinal areas (27). Evaluation of systemic inflammation can provide information about the effectiveness of the surgical procedure and the postoperative recovery in LD (4). Novel studies have provided evidence of a significant relationship between hematological parameters and inflammatory conditions in various diseases (13). In particular, the effectiveness of new platelet-related inflammation parameters such as mean platelet volume (MPV), platelet-to-lymphocyte ratio (PLR), and neutrophil-to-lymphocyte ratio (NLR) before and after inflammation and the surgical intervention have been the subject of research, achieving significant results (9).

Recent studies report the systemic immune inflammation index (SII) and systemic inflammatory response index (SIRI), calculated through the proportionality of neutrophils, monocytes, and lymphocytes (18,24,25). Furthermore, multi inflammatory index (MII) and prognostic nutrition index (PNI), which contain CRP, a chronic inflammatory marker, and albumin, a negative acute phase reactant, in addition to hematological parameters, thus having much stronger parameters for systemic inflammatory conditions (3,5,12). Evaluating these new indices together before and after surgery, which have not yet been investigated in spinal surgery, may provide meaningful results that benefit surgeons in assessing the systemic inflammatory conditions of this patient group.

The present study aimed to evaluate the efficiency of MII, PNI, SII, and SIRI indices in LD and to compare them with the previously determined inflammation-related hematological index assessing systemic inflammation in LD.

MATERIAL and METHODS

Study Design

The current analysis was a retrospective, cross-sectional, single-center study involving 105 consecutive patients who underwent surgery for LD at the Department of Neurosurgery between June 2019 and 2022. The study was approved by the Institutional Review Board and performed following the institutional guidelines and the Helsinki Declarations (No: E-96317027-514.10-232780211; Date:29.12.2023). Moreover, no formal consent was required for the study.

The study comprised three groups: Group I included data from healthy participants, Group II included data before LD, and Group III included data after LD. We analyzed and compared the measurements of the three groups, scales, and novel inflammatory indices (MPV, NLR, PLR, PNI, MII-1, MII-2, SII, and SIRI). We also assessed all the characteristics, demographic data, comorbidities, and medical history.

Participants

The inclusion criteria were rigorous to reduce bias due to the retrospective analysis. Among 1,255 LD surgeries, 162 patients who met the requirements were included in the study, along with 144 healthy individuals who were matched for age and gender. The control group in this study comprised of individuals who applied to our clinic but had no clinical problems, and were seletcted by examining patient files and laboratory results in the hospital archive. Our inclusion criteria were: patients who underwent surgery for single-segment lumbar disc herniation; compatible with the diagnosis of CT, MRI, and other imaging examinations for LD, and patients aged over 18 years who were metabolically or systemically healthy except for LD. We excluded from the study participants with these conditions that may affect hematological parameters: taking immunosuppressive drugs, infection, cardiopulmonary dysfunction or systemic diseases (DM, HT, etc.), spinal deformity or lumbar stenosis, two or more segments of lumbar herniation, or a history of surgery.

Outcome Measures

We preferred using the Roland–Morris Disability Questionnaire (RMDQ) and the Oswestry Disability Index (ODI) to assess the functional status of our participants, as they focus on pain and daily life (7). The RMDQ, consisting of 24 items covering various aspects of everyday life, is a power scale for back pain. ODI provides us with a functional disability score. It is a 10-part questionnaire in which patients with low back pain score themselves, consisting of one suitable item for assessing low back pain, and nine for assessing limitations of various activities in daily life. (11). Leg pain was evaluated preoperatively and during the last follow-up using the visual analog scale (VAS) (8). We collected RMDQ, ODI, and VASLeg preoperatively and postoperatively.

Hematologic Data and Index

Laboratory measurements included leukocyte, neutrophil, lymphocyte, monocyte, and platelet counts (SYSMEX Hemogram Autoanalyzer) as well as serum albumin and CRP (Cobas6000 Biochemistry Autoanalyzer). MII-1 (CRPx platelet-to-lymphocyte) and MII-2 (CRPx neutrophil-to-lymphocyte) were calculated manually. NLR was calculated by the proportion of neutrophils to lymphocytes, while PLR was the proportion of the platelets to lymphocytes. We calculated SII as platelet × neutrophil/lymphocyte and SIRI through [(neutrophil × monocyte)/ lymphocyte)].

Statistical Analysis

SPSS version 24 was used for statistical analysis in this study (Windows, IBM, NY, USA), while the Grandprism-v9 program (GraphPad, San Diego, CA, USA) was used to design the graphics. Patient data are presented in the table and text as mean with standard deviation for showed normally distributed continuous data, and as percentages and frequencies for categorical data. In this study, all parameters for the three groups were compared with ANOVA, while the paired-sample test was used in the dual analysis of preoperative and postoperative alterations. We performed ANOVA Tukey-b posthoc for pairwise comparisons in these groups, and the p-value was plotted on the graph, rather than in the table, for more apparent visualization. The distribution of the data was assesses using the Shapiro-Wilk-test, and Pearson Chi-square and Fisher's precision tests were used to evaluate the relationships between qualitative variations. A receiver operating characteristic (ROC) curve was used to determine the optimal cut-off for postoperative LD, and we considered p<0.05 as a significant value in all data analyses.

RESULTS

Scale Comparisons

The detailed demographic data, radiological measures, scale, and laboratory results are displayed in Table I. In the comparison of the three groups, demographic values were similar (p>0.05), while other variables showed a difference (p<0.001). In the paired analysis of scales, ODI (p<0.0001), RMDQ (p<0.0001), and VASLeg (p<0.0001) measurements decreased significantly after LD. On the contrary, the WD measurement increased (p<0.0001) as expected.

Index Comparisons

In the paired analysis of laboratory results, CRP and MPV values were similar between the preoperative and postoperative periods (p=0.489). As seen in Table I, the NLR, PLR, SII, and SIRI indices increased in postoperative measurements (p<0.0001). On the contrary, the PNI index decreased significantly with surgery (p<0.0001). There was no significant postoperative change in the measurements of MII-1 (p=0.827) and MII-2 (p=0.991). The comparison of all subgroups (*control, preoperative, and postoperative*) with the p values are displayed in Figure 1A and B.

Correlation Analysis

ODI, WD, RMDQ, and VASLeg did not correlate with parameters including NLR, PLR, MPV, PNI, and SII (p>0.05). On the contrary, ODI, WD, RMDQ, and VASLeg showed significant correlations with MII-1, MII-2, and SIRI. MII-1 had a positive relationship with ODI (r=0.259; p<0.001), RMDQ (r=0.231; p<0.001), and VASLeg (r=0.194; p < 0.001), and a negative relationship with WD (r=–0.272; p < 0.001). Similarly, MII-2 had a positive correlation with ODI (r=0.213; p<0.001), RMDQ (r:0.192; p<0.001), and VASLeg (r:0.154; p<0.001), and a negative correlation with WD (r=–0.21; p<0.001). SIRI did not correlate with VASLeg, had a positive correlation with ODI (r=0.147; p=0.001) and RMDQ (r=0.127; p=0.005), and a negative correlation with WD (r=–0.231; p<0.001).

Table I: Demographics, Measurements and Index Values of Patient Groups

Variables*	Healthy	Preoperative	Postoperative	p-value
Age, *years*	47.7 ± 15.2	49.1 ± 12.5	49.1 ± 12.5	0.622
Gender, *m/f*	78 / 68	85 / 77	85 / 77	0.715
BMI, *kg/m²*	26.9 ± 6.85	28.4 ± 4.1	28.4 ± 4.1	0.281
LL, *measurement* ° - ∟	63.8 ± 6.16	46.6 ± 13.7	46.6 ± 13.7	0.841
PI, *measurement* ° - ∟	54.9 ± 9.54	59.1 ± 12.4	59.2 ± 12.3	0.998
SS, *measurement* ° - ∟	40 ± 6.92	35.3 ± 10	35.3 ± 10	0.738
PT, *measurement* ° - ∟	14.8 ± 3.92	23.8 ± 6.26	23.8 ± 6.26	0.999
ODI, *scale*	0.3 ± 0.7	75.9 ± 18.4	25.8 ± 19.8	**0.001**
WD, *scale*	1000 ± 0	84.1 ± 112.8	465 ± 273	**0.001**
RMDQ, *scale*	0 ± 0	19.7 ± 5.2	6.2 ± 6.7	**0.001**
VASLeg, *scale*	0 ± 0	9.4 ± 1.1	1.6 ± 2.4	**0.001**
CRP, *mg/dL*	1.3 ± 2.3	4.16 ± 5.36	3.58 ± 3.7	0.489
NLR, *index*	1.6 ± 0.68	2.74 ± 3.41	5.58 ± 3.83	**0.001**
PLR, *index*	114 ± 24.6	121.3 ± 37.2	170 ± 77.8	**0.001**
PNI, *index*	42.8 ± 2.6	43.7 ± 3.1	41.6 ± 3.7	**0.001**
MII-1, *index*	184 ± 334.1	488 ± 723.9	505.2 ± 655	0.827
MII-2, *index*	1.3 ± 1.5	17.8 ± 58.7	17.8 ± 23	0,991
SII, *index*	631 ± 484	790 ± 980	1438 ± 992	**0.001**
SIRI, *index*	0.8 ± 0.4	1.6 ± 1.7	2.4 ± 1.8	**0.001**

***ODI:** Oswestry Disability Index, **PI:** Pelvic Incidence; **PT:** Pelvic Tilt; **SS:** Sacral Slope, **RMDQ:** Roland-Morris Disability Questionnaire, **VASLeg:** Visual Analog Scale for leg, **WD:** Walking Distance. Data analysis. ANOVA (three groups) was used for age, gender and BMI, while the independent Paired-samples test (preop-postop) was used for other parameters. ***:** All values for variables are given as mean ± standard deviation.*

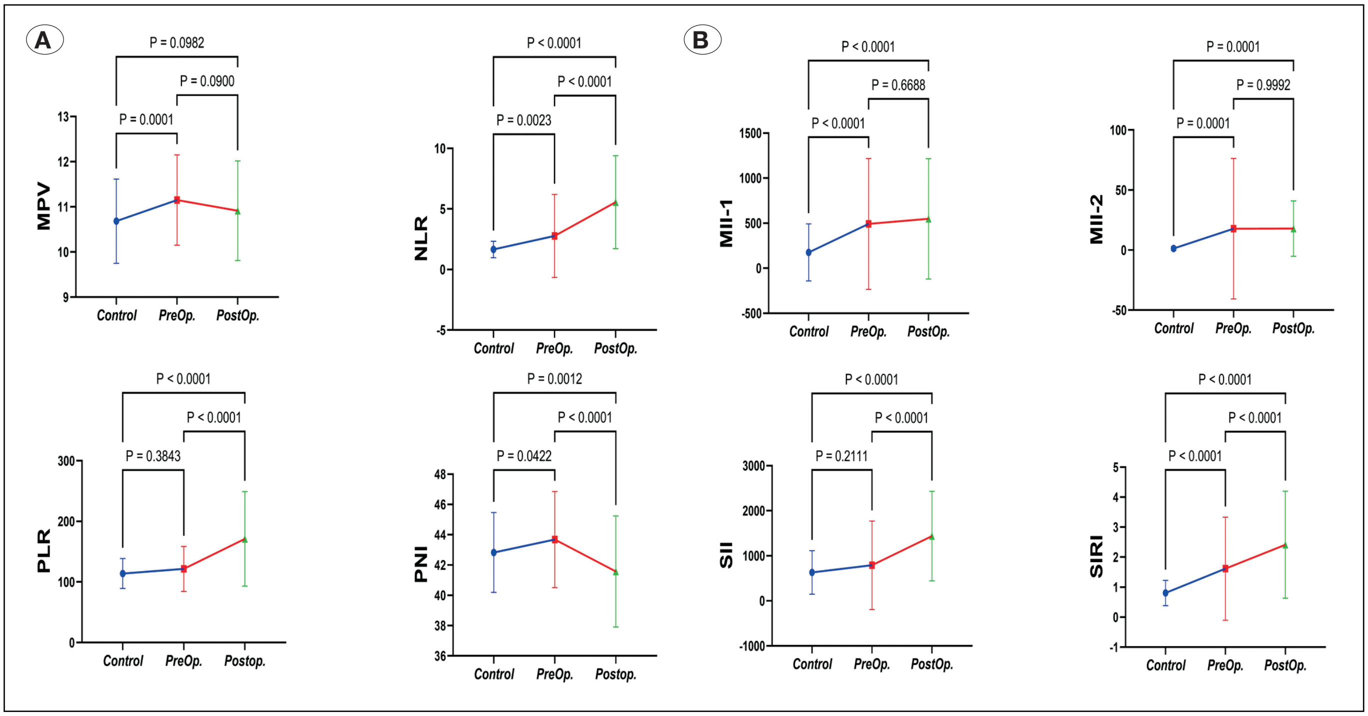

Figure 1: Displays the group comparisons for various indices where **A)** represents Neutrophil-to-Lymphocyte Ratio (NLR), Mean Platelet Volume (MPV), Platelet-to-Lymphocyte Ratio (PLR), and Prognostic Nutritional Index (PNI), and **B)** stands for Multi-Inflammatory Index 1 (MII-1), Multi-Inflammatory Index 2 (MII-2), Systemic Immune-Inflammation Index (SII), and Systemic Inflammatory Response Index (SIRI).

ROC Analysis

Figure 2 demonstrates that MPV (p = 0.645) and PNI (p=0.105) did not show a significant value for LD in the ROC. NLR (p<0.001), SII (p<0.001), and SIRI (p<0.001) were the most substantial indices in all for LD surgery (Table II). PLR (p<0.001), MII-1 (p=0.004), and MII-2 (p<0.001) were also found to be valuable indices for the LD. The cut-off value of NLR was 2.71, with a 78% sensitivity and 83.2% specificity value. The cut-off value of SII was 780, with a 72.3% sensitivity and 79.4% specificity, while that of SIRI was 1.28, with a 76.4% sensitivity and 77.3% specificity.

DISCUSSION

The present study assessed the effectiveness of new inflammatory indices for the preoperative and postoperative periods of LD by making comparisons with healthy controls. These indices may provide insight on the clinical use of LD surgery for inflammatory conditions in the preoperative and postoperative periods. In particular, MII-1, MII-2, SII, and SIRI provided evidence that they have significant benefits, such as NLR for patients with LD.

Although the efficacy of inflammation in spinal surgery is known, research initiated by Takahashi et al. analyzed the kinetics of lymphocytes in patients undergoing spinal surgery (22). Afterward, a series of studies focused on the clinical importance of hematological sub-parameters and indices such as NLR and PLR. New publications have emerged on

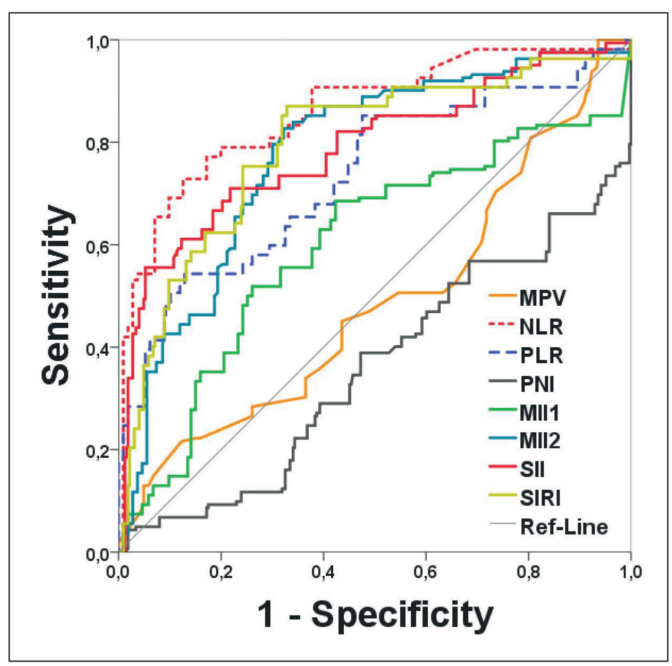

Figure 2: ROC curve for indices predicting postoperative lumbar discectomy: Neutrophil-to-Lymphocyte Ratio (NLR), Mean Platelet Volume (MPV), Platelet-to-Lymphocyte Ratio (PLR), and Prognostic Nutritional Index (PNI), Multi-Inflammatory Index 1 (MII-1), Multi-Inflammatory Index 2 (MII-2), Systemic Immune-Inflammation Index (SII), and Systemic Inflammatory Response Index (SIRI).

Table II: Comparison of Indices for Predicting Postoperative Lumbar Discectomy

Variables	AUC	SE	p-value	95% CI	
				Lower	Upper
MPV	0.487	0.029	0.645	0.431	0.544
NLR	0.859	0.019	**0.0001**	0.822	0.897
PLR	0.734	0.026	**0.0001**	0.684	0.784
PNI	0.358	0.028	0.105	0.304	0.412
MII-1	0.598	0.029	**0.0004**	0.541	0.656
MII-2	0.777	0.022	**0.0001**	0.733	0.821
SII	0.788	0.024	**0.0001**	0.742	0.834
SIRI	0.794	0.023	**0.0001**	0.749	0.838

MII: *Multi Inflammatory Index,* ***NLR:*** *Neutrophil-to lymphocyte-ratio,* ***PLR:*** *Platelet-to-lymphocyte ratio, SII: Systemic immune-inflammation index, SIRI: Systemic inflammatory response index, PNI: Prognostic nutrition index,* ***MPV:*** *Mean Platelet Volume,* ***AUC:*** *Area Under the Curve,* ***SE:*** *Standart error,* ***CI:*** *Confidence Interval.*

spinal surgery and on different inflammation-related diseases (2). A good proportion of routine tests calculated these new indices, and although many brain surgeons take a distant stance against them, novel reports proved that they would be beneficial over time (16,19). SII and SIRI, accepted as new and more complex forms of NLR and PLR, have not yet been investigated in spinal surgery and LD.

SIRI, a new inflammation-based index calculated with neutrophil, lymphocyte, and monocyte counts, was found to reflect the inflammatory response and to have a prognostic value in many diseases, including cancers (20). Similarly, SII, the recent subject of widespread research, was also stated to predict outcomes in several types of malignancies (6). This new index, obtained using hematological parameters such as SIRI that provide information on inflammatory processes, is increasingly being accepted as a ready biomarker for systemic inflammation (14,23,26). They have the potential to better reflect the inflammatory states that occur in diseases separately from NLR, PLR, and MPV. In the present study, SII and SIRI showed a substantial and valuable difference for LD surgery. NLR, PLR, SII, and SIRI increased in postoperative measurements. According to the ROC, NLR, SII, and SIRI were the most vital indices for surgery, with high sensitivity and specificity. Instead, PLR and MPV were invalid parameters for the LD.

In the paired analysis of laboratory results, CRP and MPV values were similar between the preoperative and postoperative periods. In LD surgery, we do not expect significant changes in CRP in a brief period. However, the result differed for MII-1 and MII-2, in which CRP was combined with lymphocytes and neutrophils. For these newly explored indices, Ferit considered the systemic inflammatory response to be critically important (3). Similar to this relationship, Iwata et al. showed that lower postoperative lymphocyte count and higher CRP level might be helpful to screen patients undergoing lumbar spinal surgery (15). In our study, there was no significant postoperative change in the measurements of MII-1 and MII-2. MII-1 and MII-2 were relevant for LD surgery, but not as significant as SIRI and SII. Although it is an index combined with CRP and albumin, PNI did not show a significant difference for LD surgery in the ROC analysis.

In this study, positive alterations were achieved as expected in the scales used to measure the efficacy of the LD surgery. In the paired analysis of scales, ODI, RMDQ, and VASLeg measurements decreased, whereas the WD measurement increased after the LD, as expected. The scales did not show a correlation with parameters including NLR, PLR, MPV, PNI, and SII in the analysis. On the contrary, MII-1, MII-2, and SIRI showed a positive correlation with ODI, RMDQ, and VASLeg, and a negative correlation with WD.

The most substantial aspect of the study is that these new indexes were analyzed for the first time in LD surgeries. In addition, these analyses were compared with similar indices that had previously been shown to be useful, and their effectiveness was compared with them. As a significant limitation, the long-term efficacy of these indices was lacking, as all patient data did not include long-term follow-up. Building on previous studies, the present study attempted to understand these parameters through inflammation mechanisms. Hematological indices or parameters generally increase inflammation-related events and may lead to a bias. Of course, the response of these indices is not the same in every inflammation-related disease. In this sense, the study wanted to analyze which new indices changed, especially for LD patients, compared to preoperative/postoperative and healthy individuals. To minimize bias caused by the widespread effect of inflammation, we were very selective during and included only participants with isolated LD into the patient group. A more extensive study with a more homogeneous patient group may have yielded different results.

CONCLUSION

NLR, SII, and SIRI were the most substantial and valuable indices for assessing the inflammatory condition in LD. Regarding superiority to SII and NLR, SIRI showed significant agreement with the scales for LD. On the other hand, MII-1 and MII-2 showed a strong correlation with the scales but remained less valuable for LD, while MPV and PNI were the most inconsistent and weakly practical tests for LD among these indices. SIRI and SII, which showed strong efficacy in the present study, need more comprehensive and prospective analyses to be used in monitoring inflammation activity in LD during follow-up.

AUTHORSHIP CONTRIBUTION

The author (SD) confirm responsibility for the following: study conception and design, data collection, analysis and interpretation of results, and manuscript preparation.

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