TIBBIYOT
TA'LIMI & INNOVATSIYALARI



- 14.00.00 - Tibbiyot fanlari;
- 14.00.01 - Akusherlik va ginekologiya;
- 14.00.02 - Morfologiya;
- 14.00.03 - Endokrinologiya;
- 14.00.04 - Otorinolaringologiya;
- 14.00.05 - Ichki kasalliklar;
- 14.00.06 - Kardiologiya;
- 14.00.07 - Gigiena;
- 14.00.08 - Oftal'mologiya;
- 14.00.09 - Pediatriya;
- 14.00.10 - Yuqumli kasalliklar;
- 14.00.11 - Dermatologiya va venerologiya;
- 14.00.12 - Tibbiy reabilitologiya;
- 14.00.13 - Nevrologiya;
- 14.00.14 - Onkologiya;
- 14.00.15 - Patologik anatomiya;
- 14.00.16 - Normal va patologik fiziologiya;
- 14.00.17 - Farmakologiya va klinik farmakologiya;
- 14.00.18 - Psixiatriya va narkologiya;
- 14.00.19 - Klinik radiologiya;
- 14.00.20 - Tibbiy genetika;
- 14.00.21 - Stomatologiya;
- 14.00.22 - Travmatologiya va ortopediya;
- 14.00.23 - Hamshiralik ishini tashkil etish;
- 14.00.24 - Sud tibbiyoti;
- 14.00.27 - Xirurgiya;
- 14.00.28 - Neyroxirurgiya;
- 14.00.41 - Xalq tabobati;
- 14.00.35 - Bolalar xirurgiyasi;
- 14.00.34 - Yurak-qon tomir xirurgiyasi

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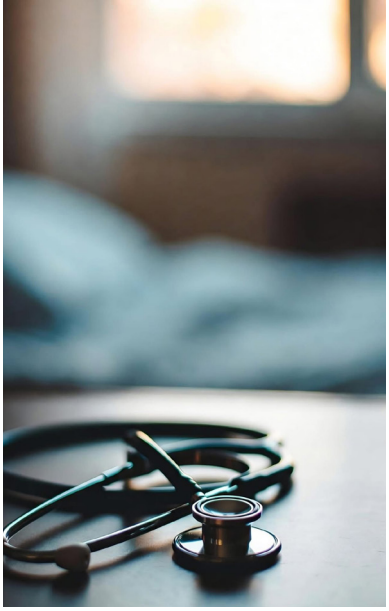
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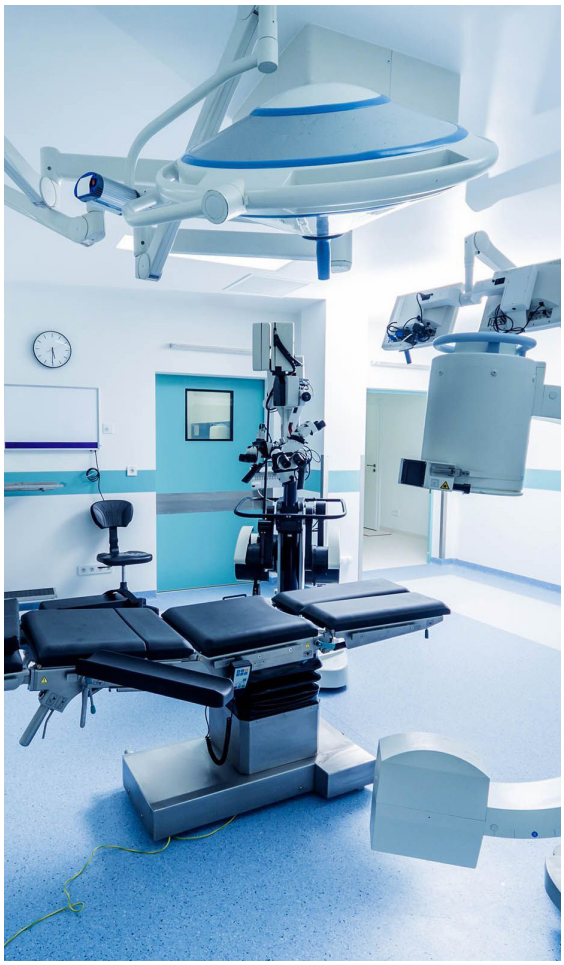
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Tahrir hay’ati a’zolari:



BOSH MUHARRIR:
Shuhrat Baymuradov Abdujalilovich
tibbiyot fanlari doktori (DSc), professor



BOSH MUHARRIR O‘RINBOSARI:
Iminov Komiljon Odiljonovich
tibbiyot fanlari bo‘yicha falsafa doktori

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Tahrir hay’ati a’zolari:



Sharipov Kongratbay Avezimbetovich
Texnika fanlari doktori (DSc), professor



Ishanqulov Artiqboy Eshboyevich
Biologiya fanlari doktori (DSc), professor



Otamuradov Furqat Abdukarimovich
tibbiyot fanlari doktori (DSc), dotsent.



Shuxrat Jumayevich Teshayev
tibbiyot fanlari doktori (DSc), professor



Oral Aminovna Ataniyazova
tibbiyot fanlari doktori (DSc), professor



Jalolova Feruza Maxamatjanovna
Tibbiyot fanlari bo‘yicha falsafa doktori (DSc), dotsent



Uraqov Shokir Ulashovich
tibbiyot fanlari doktori doktori (DSc)

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Murojaat uchun telefon:
+998 97 748 70 03
Email: @munis_sm

MUNDARIJA

SEREBROVASKULYAR KASALLIKLARDA BUYRAK SHIKASTLANISHINING ISHEMIK-GIPOKSIK MEXANIZMLARI: HIF-1α VA TGF-β1 KO‘RSATKICHLARINING YOSHGA BOG‘LIQ O‘ZGARISHLARI 16
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DISCRIMINATIVE PERFORMANCE OF HEMATOLOGICAL PARAMETERS FOR IDENTIFYING B-THALASSEMIA CARRIERS: A SECONDARY ANALYSIS OF AN OPEN-ACCESS SCREENING DATASET



Alimov Farruh Shuhrat ugli
Student of Tashkent medical university
E-mail: farruhalimov2006@icloud.com

Abstract: β-thalassemia is an inherited hemoglobin disorder characterized by reduced or absent β-globin chain production. Individuals with β-thalassemia trait are usually clinically asymptomatic or have mild hematological abnormalities, but their laboratory profile may overlap with other causes of microcytosis. To compare hematological parameters between individuals classified as normal and β-thalassemia carriers and to assess the discriminatory performance of selected parameters using receiver operating characteristic (ROC) analysis. A secondary analysis was performed using an open-access hematological screening dataset containing complete blood count and hemoglobin analysis results. The analysis included 12,345 participants: 11,783 classified as normal and 562 classified as β-thalassemia carriers. Hb, RBC, MCV, MCH, MCHC, HbA2, and HbF were compared using the Mann–Whitney U test. ROC analysis was performed for MCV, HbA2, MCH, and RBC. The carrier group had lower Hb, MCV, and MCH and higher RBC, HbA2, and HbF than the normal group. MCV had an AUC of 0.956, HbA2 0.953, MCH 0.948, and RBC 0.788. MCV, MCH, and HbA2 showed strong discriminatory performance for identifying β-thalassemia carriers. The derived cutoffs may support preliminary screening but require validation in independent populations.

Key words: β-thalassemia trait; β-thalassemia carrier status; complete blood count; MCV; MCH; HbA_2

Annotatsiya: β-talassemiya irsiy gemoglobinopatiya bo‘lib, β-globin zanjirlarining kamayishi yoki yo‘qligi bilan tavsiflanadi. β-talassemiya tashuvchilari odatda klinik jihatdan simptomsiz yoki yengil gematologik o‘zgarishlarga ega bo‘ladi, biroq ularning laborator ko‘rsatkichlari mikrositozning boshqa sabablarida kuzatiladigan ko‘rsatkichlarga o‘xshashi mumkin. Tadqiqotning maqsadi normal guruh va β-talassemiya tashuvchilari o‘rtasidagi gematologik ko‘rsatkichlarni taqqoslash hamda tanlangan ko‘rsatkichlarning diskriminativ imkoniyatlarini ROC tahlili yordamida baholashdan iborat. Ochiq kirishli gematologik skrining ma’lumotlar to‘plamining ikkilamchi tahlili o‘tkazildi. Tahlilga 12 345 ishtirokchi: 11 783 nafar normal guruh vakili va 562 nafar β-talassemiya tashuvchisi kiritildi. Hb, RBC, MCV, MCH, MCHC, HbA2 va HbF ko‘rsatkichlari Mann–Whitney U testi yordamida taqqoslandi; MCV, HbA2, MCH va RBC uchun ROC tahlili o‘tkazildi. Tashuvchilarda Hb, MCV va MCH ko‘rsatkichlari past, RBC, HbA2 va HbF ko‘rsatkichlari esa yuqori bo‘ldi. MCV uchun AUC 0,956, HbA2 uchun 0,953, MCH uchun 0,948 va RBC uchun 0,788 ni tashkil etdi. MCV, MCH va HbA2 β-talassemiya tashuvchilarini ajratishda yuqori diskriminativ ko‘rsatkichlarni namoyon qildi. Aniqlangan chegaraviy qiymatlar dastlabki skrining uchun foydali bo‘lishi mumkin, biroq ularni klinik amaliyotga joriy etishdan oldin mustaqil populyatsiyalarda validatsiya qilish zarur.

Kalit so‘zlar: β-talassemiya tashuvchiligi; talassemiya tashuvchisi; umumiy qon tahlili; MCV; MCH; HbA_2

Аннотация: β-талассемия является наследственной гемоглобинопатией, характеризующейся снижением или отсутствием продукции β-глобиновых цепей. Носители β-талассемии обычно клинически бессимптомны или имеют лёгкие гематологические изменения, однако их лабораторный профиль может перекрываться с другими причинами микроцитоза. Целью исследования было сравнить гематологические показатели между лицами, классифицированными как здоровые, и носителями β-талассемии, а также оценить дискриминационную

способность отдельных показателей с помощью ROC-анализа. Проведён вторичный анализ общедоступного набора данных гематологического скрининга. В анализ включены 12 345 участников: 11 783 человека из группы нормы и 562 носителя β-талассемии. Сравнивали Hb, RBC, MCV, MCH, MCHC, HbA2 и HbF с использованием U-критерия Манна–Уитни; для MCV, HbA2, MCH и RBC проведён ROC-анализ. У носителей отмечались более низкие показатели Hb, MCV и MCH и более высокие показатели RBC, HbA2 и HbF. AUC составила 0,956 для MCV, 0,953 для HbA2, 0,948 для MCH и 0,788 для RBC. MCV, MCH и HbA2 продемонстрировали высокую дискриминационную способность для выявления носителей β-талассемии. Полученные пороговые значения могут быть полезны для предварительного скрининга, однако требуют валидации в независимых популяциях.

Ключевые слова: β-талассемия; носительство β-талассемии; общий анализ крови; MCV; MCH; HbA_2

INTRODUCTION

β-thalassemia is an inherited disorder of hemoglobin synthesis caused by reduced or absent production of β-globin chains. It is among the most common monogenic disorders worldwide and occurs with particularly high frequency in several regions of the Mediterranean, the Middle East, South Asia, and Southeast Asia. The clinical and hematological manifestations vary according to the underlying genetic variant and the number of affected β-globin alleles. β-thalassemia trait, also known as the carrier state, is generally associated with a mild phenotype and is often identified during routine hematological investigations. Typical laboratory findings include reduced mean corpuscular volume (MCV), reduced mean corpuscular hemoglobin (MCH), and a relatively increased red blood cell (RBC) count. An increased proportion of hemoglobin A_2 (HbA_2) is also an important laboratory feature supporting the identification of β-thalassemia carriers [1–3]. Differentiating β-thalassemia trait from other causes of microcytosis, particularly iron deficiency, is clinically important. Incorrect classification may result in inappropriate treatment and missed opportunities for genetic counseling and carrier detection. Although hemoglobin analysis by high-performance liquid chromatography (HPLC) or electrophoresis and molecular testing can provide more definitive information, these methods may not be readily available in all healthcare settings. Consequently, routinely available hematological parameters can be valuable for preliminary screening and identifying individuals who require further investigation [3–6].

Several erythrocyte parameters and derived indices have been investigated for differentiating thalassemia carriers from iron deficiency and other causes of microcytosis. In particular, MCV, MCH, and RBC count have demonstrated useful discriminatory characteristics in previous studies, although their performance may vary between populations. HbA_2 measurement remains an important component of the laboratory evaluation of β-thalassemia trait [4–8]. Receiver operating characteristic (ROC) analysis provides a useful method for evaluating the ability of individual laboratory parameters to discriminate between two diagnostic groups. Assessment of the area under the ROC curve (AUC), together with sensitivity and specificity at selected thresholds, can help identify parameters with the greatest discriminatory potential. The present study aimed to compare routinely available hematological and hemoglobin-related parameters between individuals classified as normal and β-thalassemia carriers using an open-access screening dataset. A further objective was to evaluate the discriminatory performance of MCV, MCH, RBC count, and HbA_2 using ROC analysis. The findings may help clarify the potential value of commonly available laboratory parameters as preliminary indicators of β-thalassemia carrier status.

LITERATURE REVIEW

The present secondary analysis demonstrated clear differences in hematological and hemoglobin-related parameters between individuals classified as normal and those classified as β-thalassemia carriers. The most prominent findings were lower MCV and MCH values, a higher RBC count, and substantially increased HbA_2 levels among β-thalassemia carriers. This pattern is consistent with the characteristic hematological profile associated with β-thalassemia trait [1–4]. The carrier group had a markedly lower MCV than the normal group (67.80 ± 5.97 vs. 86.65 ± 7.89 fL). MCH was also substantially lower among carriers. Microcytosis and hypochromia are recognized laboratory features of β-thalassemia trait and reflect impaired β-globin synthesis [1–3]. The strong discriminatory performance of MCV in the present analysis (AUC 0.956) suggests that this routinely available parameter may be useful for identifying individuals who warrant further investigation. The RBC count was higher among β-thalassemia carriers than among individuals classified as normal. A relatively preserved or increased RBC count in the presence of marked microcytosis is a recognized feature of thalassemia trait and has been incorporated into several screening indices [4–7]. However, the lower AUC observed for RBC count in the present study (0.788), compared with MCV and MCH, suggests that RBC count alone may be insufficient for reliable discrimination.

HbA_2 demonstrated excellent discriminatory performance in the present analysis, with an AUC of 0.953. The mean HbA_2 concentration was considerably higher in the carrier group (5.31 ± 0.52%) than in the normal group (2.96 ± 0.30%). Increased HbA_2 is an important laboratory finding supporting the diagnosis of β-thalassemia trait, although its interpretation may be affected by factors such as iron deficiency and other hemoglobin variants [3,8]. The ROC analysis showed particularly strong performance for MCV, HbA_2, and MCH. These findings are broadly consistent with previous studies evaluating erythrocyte indices and hemoglobin parameters for thalassemia screening [4–7]. Nevertheless, the cutoff values identified in the present analysis should not be interpreted as universal clinical thresholds because they were derived from a specific secondary dataset. Validation in independent populations is required before such thresholds can be applied clinically. The lower hemoglobin concentration observed among carriers should also be interpreted cautiously. β-thalassemia trait is generally associated with a mild hematological phenotype, but hemoglobin levels can vary according to an individual's genetic background and the presence of additional conditions. Therefore, hemoglobin concentration alone cannot reliably distinguish β-thalassemia trait from iron deficiency or other causes of anemia [2,3,8].

This study has several limitations. First, the analysis was based on a previously collected open-access dataset, and information regarding the original sampling strategy and laboratory procedures was determined by the original data source rather than by the present investigators. Second, detailed demographic and clinical information was not available for the present analysis, limiting assessment of potential confounding factors. Third, the analyzed groups were defined according to the diagnostic classification provided in the dataset and should not be interpreted as representative prevalence estimates for the general population. Finally, the ROC-derived thresholds require external validation. Despite these limitations, the findings indicate that routinely available hematological parameters, particularly MCV, MCH, and HbA_2, can provide substantial discriminatory information for identifying individuals classified as β-thalassemia carriers. These parameters may therefore be useful in preliminary screening strategies, particularly in settings where advanced diagnostic methods are less accessible. Definitive diagnosis, however, should rely on appropriate hemoglobin analysis and, when indicated, molecular genetic testing [2,3].

RESEARCH METHODOLOGY

This study was conducted as a secondary analysis of an open-access hematological screening dataset containing complete blood count and hemoglobin analysis data. The dataset was obtained from the publicly available HPLC-Based Thalassemia Screening Data repository hosted on Kaggle. The present analysis used previously collected and anonymized records; no new biological samples were collected. The dataset contained 13,031 records. For the present two-group analysis, 12,345 records were included: 11,783 individuals classified as normal and 562 individuals classified as β-thalassemia carriers according to the diagnostic categories provided in the dataset. The remaining records represented other diagnostic categories and were excluded from this comparison. The following parameters were evaluated: hemoglobin (Hb), red blood cell count (RBC), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), hemoglobin A_2 (HbA_2), and fetal hemoglobin (HbF).

Continuous variables were summarized as mean ± standard deviation (SD). Differences between the normal and β-thalassemia carrier groups were evaluated using the Mann–Whitney U test. A two-sided p-value <0.05 was considered statistically significant. ROC curve analysis was performed to assess the discriminatory performance of MCV, MCH, RBC count, and HbA_2. The area under the ROC curve (AUC), sensitivity, and specificity were calculated. The optimal cutoff was determined using the Youden index. Statistical analyses were performed using Python with standard scientific and statistical computing libraries. This study involved a secondary analysis of an existing open-access and anonymized dataset and did not involve direct recruitment of participants or collection of new biological samples. The data-use conditions and licensing requirements associated with the public dataset were respected.

ANALYSIS AND RESULTS

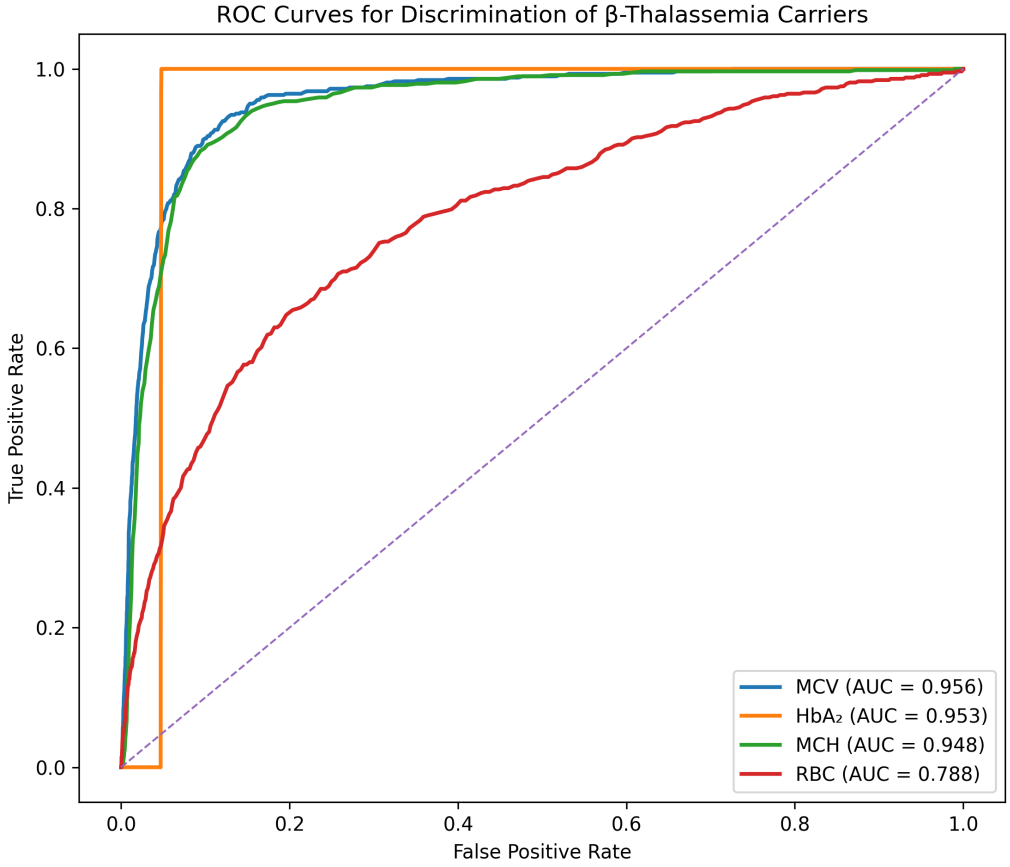
A total of 13,031 records were available in the dataset. For the present analysis, 12,345 records were included, comprising 11,783 individuals classified as normal and 562 individuals classified as β-thalassemia carriers. The remaining records represented other diagnostic categories and were not included in the two-group comparison. The β-thalassemia carrier group had a lower mean hemoglobin (Hb) concentration than the normal group (10.52 ± 1.57 vs. 11.91 ± 1.74). In contrast, the mean red blood cell (RBC) count was higher among carriers (5.08 ± 0.77 vs. 4.27 ± 0.66). Marked differences were observed in erythrocyte indices. Mean corpuscular volume (MCV) was substantially lower among β-thalassemia carriers than in the normal group (67.80 ± 5.97 vs. 86.65 ± 7.89 fL). Similarly, mean corpuscular hemoglobin (MCH) was lower among carriers

(20.63 ± 2.45 vs. 28.12 ± 3.52 pg). In contrast, hemoglobin A_2 (HbA_2) was markedly higher among carriers (5.31 ± 0.52 vs. 2.96 ± 0.30%), while fetal hemoglobin (HbF) was also higher (1.04 ± 0.85 vs. 0.44 ± 0.34%). According to the Mann–Whitney U test, differences between the normal and β-thalassemia carrier groups were statistically significant for all evaluated parameters ($p < 0.001$). However, MCHC demonstrated substantial variability in the carrier group (31.25 ± 16.83), and this finding should therefore be interpreted cautiously.

Receiver operating characteristic (ROC) analysis demonstrated excellent discriminatory performance for MCV, HbA_2, and MCH.

MCV showed an area under the curve (AUC) of 0.956. At an optimal cutoff of ≤76.6 fL, sensitivity was 92.5% and specificity was 87.9%. HbA_2 demonstrated an AUC of 0.953. At an optimal cutoff of ≥4.0%, sensitivity was 100.0% and specificity was 95.2%. MCH showed an AUC of 0.948, with a sensitivity of 89.2% and specificity of 89.7% at an optimal cutoff of ≤23.5 pg. RBC count demonstrated comparatively lower discriminatory performance, with an AUC of 0.788. At an optimal cutoff of ≥4.86 × 10^6/μL, sensitivity was 64.8% and specificity was 80.4%. Overall, MCV, HbA_2, and MCH demonstrated excellent discriminatory performance for distinguishing participants classified as β-thalassemia carriers from those classified as normal in the analyzed dataset.

Table 1. Comparison of hematological parameters between normal participants and β-thalassemia carriers



CONCLUSION

This secondary analysis demonstrated substantial differences in hematological parameters between individuals classified as normal and β-thalassemia carriers. β-thalassemia carriers showed lower MCV and MCH values, a higher RBC count, and markedly higher HbA_2 concentrations. Among the evaluated parameters, MCV, HbA_2, and MCH demonstrated excellent discriminatory performance, whereas RBC count showed moderate discriminatory ability. These findings suggest that routinely available hematological parameters may be useful for the preliminary identification of individuals who require further evaluation for β-thalassemia trait. However, the cutoff values obtained in this analysis should be validated in independent, clinically characterized populations before clinical application. Hemoglobin analysis and, when appropriate, molecular genetic testing remain important for definitive diagnosis.

This study involved a secondary analysis of an existing open-access and anonymized dataset. No new participants were recruited, and no biological samples were collected for the present study. The data-use conditions associated with the original dataset were respected. Ethics Statement: Not applicable. No identifiable

individual participant information was used. Data Availability Statement: The data analyzed in this study were obtained from the publicly available HPLC-Based Thalassemia Screening Data dataset hosted on Kaggle and distributed under a CC BY-SA 4.0 license. Conflict of Interest: The authors declare that they have no competing interests.

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