Artículo original

Assessing LBICO, a Bicoherence-derived Multi-frequency Index Measured from EEG Signals

Evaluación de LBICO, un índice multifrecuencia derivado de la bicoherencia medido a partir de señales EEG

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ABSTRACT

Context: The need for an EEG-based index for depth of anesthesia (DoA) assessment is widely recognized. Unfortunately, the algorithm for the gold standard DoA index, the Bispectral Index (BIS™) has not been disclosed by their creators. The importance of cross-frequency phase coupling in brain function is widely acknowledged, and we centered our study in assessing bicoherence, given its independence on amplitude-related phase coupling.

Aims: To introduce, a new, bicoherence-based index for DoA assessment (LBICO).

LBICO is based on EEG power spectrum and bicoherence ratios measured at specific frequency intervals.

Methods and Material: LBICO was tested on a publicly available database of EEG recordings with simultaneous BIS™ values from 24 patients during surgery. EEG recordings were pre-processed via Empirical Mode Decomposition (EMD) filtering and further removal of artefacts. Statistical analysis used: Simultaneous plots, correlation analysis and Bland-Altman plots for assessing agreement between LBICO and BIS™ measurements. Power spectrum and bispectrum estimation of EEG recordings.

Results: Agreement between LBICO and BIS™ was assessed by comparing 16,861 artefact-free pairs of values taken from all the 24 recordings from the database (corresponding to a total of 23.42 hours). A correlation of r=0.70 was obtained (p=0.0000).

Conclusions: These results suggest that the use of bicoherence-based indices can have both theoretical and practical implications for understanding the basic mechanisms of anaesthesia as well as patient management at the Intensive Care Settings.

Key-words: multi-frequency Index; EEG; spectrum; bispectrum; bicoherence; empirical mode decomposition; LBICO.

RESUMEN
Se reconoce ampliamente la necesidad de un índice basado en EEG para la evaluación de la profundidad de la anestesia (DoA). Desafortunadamente, el algoritmo para el índice DoA estándar de oro, el Índice Bispectral (BIS™), no ha sido revelado por sus creadores. La importancia del acoplamiento de fases de frecuencia cruzada en la función cerebral es ampliamente reconocida, y centramos nuestro estudio en la evaluación de la bicoherencia, dada su independencia del acoplamiento de fases relacionado con la amplitud.
Objetivos: Introducir un nuevo índice basado en bicoherencia para la evaluación de DoA (LBICO).
Métodos y material: LBICO se basa en el espectro de potencia del EEG y en relaciones de bicoherencia medidas en intervalos de frecuencia específicos. LBICO se probó en una base de datos disponible públicamente de registros de EEG con valores BIS™ simultáneos de 24 pacientes durante la cirugía. Los registros de EEG se procesaron previamente mediante filtrado por descomposición en modo empírico (EMD) y eliminación adicional de artefactos. Análisis estadístico utilizado: gráficos simultáneos, análisis de correlación y gráficos de Bland-Altman para evaluar la concordancia entre las mediciones de LBICO y BIS™. Estimación del espectro de potencia y biespectro de registros de EEG.
Resultados: Se evaluó la concordancia entre LBICO y BIS™ comparando 16.861 pares de valores libres de artefactos tomados de los 24 registros de la base de datos (correspondientes a un total de 23,42 horas). Se obtuvo una correlación de r=0,70 (p=0,0000).
Conclusiones: Estos resultados sugieren que el uso de índices basados en bicoherencia puede tener implicaciones tanto teóricas como prácticas para comprender los mecanismos básicos de la anestesia, así como el manejo de los pacientes en los entornos de cuidados intensivos.
Palabras clave: índice multifrequencia; EEG; espectro; biespectro; bicoherencia; descomposición en modo empírico; LBICO.

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Introduction

Electroencephalogram (EEG) bispectrum is useful for assessing brain function through cross-frequency phase coupling.(1-4)
Anaesthesiology still poses challenges (5-8), and EEG-derived indices help in Depth of Anaesthesia (DoA) assessment.(9)
The most popular DoA indexis the "Bispectral Index"(BIS™),(10) but its algorithm was not disclosed.(3)
BIS™ is correlated with anaesthesia scales, is predictive in sleep staging, and delirium detection.(3-11)
However, some discourage the use of BIS™, asking for other DoA indices considering different EEG aspects, as spectral components, entropy, etc.(15-21)
Bicoherence-derived measures are based on biophysically plausible assumptions and this motivated us to develop LBICO, a bicoherence-based index to assess DoA.

Subjects and Methods

Data

In this study we used a publicly available data set corresponding to the “supplementary material” of reference.[22]

Briefly, data corresponded to 24 patients who received surgery under general anaesthesia at The National Taiwan University Hospital. None of the participants underwent high risk operations. Patients with alcohol or smoking habits, or illness that affected the data recording, were not included. Finally, 24 patients (age (yr.): 44.5 ± 12.9, height (cm): 164.2 ± 7.1, weight (kg): 63.4 ± 14.8, and BMI (kg/m^2): 23.4 ± 4.2, gender: 14 females/10 males) were included into the database. Surgeries lasted 126.4 ± 72.9 min.

Recording Conditions

Prior to EEG recording, good contact was assured to improve the connection between the frontal scalp skin and EEG BIS™ Quatro Sensor (Aspect Medical Systems, Newton, MA, US) in order to reduce the impedance below 5 kΩ. The EEG data were acquired at a sampling rate of 128 Hz. The intermittent BIS™ value was obtained every 5 s The recording began 5 min ahead of the onset of induction, at which time patients were fully awake, and it terminated when participants began to respond to doctors either by voice or by movement. Each individual file from the database contains a continuous single-channel EEG recording at 128 Hz and a series of BIS™ values taken at 5-second intervals.

Data Pre- Processing

EEG data contained numerous artefacts resulting in waveform saturation due to electrical artefacts caused by medical equipment or body movement (see, for example, the unfiltered EEG trace in figure 1), thus considerably reducing the number of good-quality segments. A notch filter was used to remove the 60-Hz line noise. Subsequently, a 5-s data epoch was used to conduct the EMD analysis, and a 30-s segment of the reconstructed signal which was used for the LBICO calculation. The sliding window step size was set to 5-s to be consistent with the BIS™ value for further comparisons.

Filtering via Empirical Mode Decomposition

EEG signal can be easily contaminated by artefacts such as noise from diverse nature, and it is necessary to filter the signals to reduce the computation error. To reduce their effect, we applied empirical mode decomposition (EMD). Briefly, with EMD method, the EEG signal is decomposed as a sum of often small number of components. These components form a complete and nearly orthogonal basis for the original signal, and are described as intrinsic mode functions (IMF). Usually the first IMF (IMF1) carries the most oscillating (high-frequency) components, and can be rejected to remove high-frequency noise components. This decomposition is based on the local characteristic time scale of the data, and it can be applied to nonlinear and non stationary processes.[24] In other words, since EMD is based on the local characteristics of a data series, it is applicable to nonlinear and non stationary processes, thus overcoming both pseudo-linearity and stationarity. In our case we applied the Matlab EMD package developed by G. Rilling.[23] In this study the EEG signals were reconstructed by summing the components IMF2 and IMF3 after decomposition to obtain the filtered signals due to their superior discrimination ability of different states of anaesthesia, as recommended.[25] In figure 1, the result of EMD filtering to EEG data is illustrated. Both raw and EMD-filtered signals were submitted to power spectral and bispectral analysis.

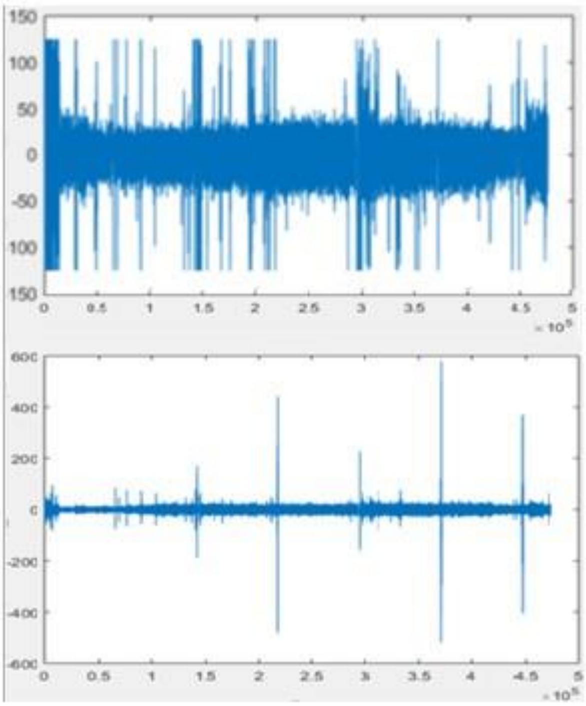

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Fig. 1- A raw EEG trace (top), and the filtered trace after application of the EMD algorithm (bottom). Note the difference in scales.

Power Spectrum and Bicoherence Estimation

In bispectral EEG analysis, the cross-bispectrum is defined as:

$$H(f_1, f_2) = \langle X(f_1)Y(f_2)Z^*(f_1 + f_2)\rangle \qquad (1)$$

In (1) <.> denotes averaging, whereas “*” is complex conjugate. X, Y and Z correspond to three simultaneously recorded signals.

In particular, the auto-bispectrum corresponds to the case when only one signal is considered (X=Y=Z). In order, to obtain a measure of the inter-frequency phase locking independent of the strength of the signal, the normalized bispectrum is identified as bicoherence. The absolute value of the bicoherence is between zero and one: A value of one corresponds to perfect coupling and zero indicates no coupling.

A useful normalization is constructed by 3-norms:

$$N(f_1,f_2) = ((|X[\![(f]\!]_1)|^3)(|X[\![(f]\!]_2)|^3)(|X[\![(f]\!]_1+f_2)|^3))^{\frac{1}{3}} \quad (2)$$

Accordingly, bicoherence is defined as

$$B(f_1,f_2) = \frac{H(f_1,f_2)}{N(f_1,f_2)} \quad (3)$$

As recommended in references. [26], [27]

Even in the case of recording from one site only, bicoherence retains a large deal of information about coupling between different neuronal networks across the brain. [26]

In particular, bispectrum derived indices have been proposed for assessing the depth of anaesthesia (DoA). In this study, instead of bispectrum, we based our analysis on bicoherence values, since bispectrum values are influenced by both the amplitude of signals as well as the degree of phase coupling.

For estimating both power spectrum and bicoherence, we used the Matlab functions “data2cs_event” and “data2bs_*univar*” respectively; these Matlab functions were developed by Guido Nolte´s Lab, and are freely available within the METH toolbox at https://www.uke.de/english/departments-institutes/institutes/neurophysiology-and-pathophysiology/research/research-groups/index.html

For power spectrum estimation, the function “data2cs_event” from the METH toolbox was used.

For bicoherence estimation (see formulas 1-3), we used the Matlab function “data2bs_univar” from the METH toolbox. Each analysed ECG segment was 30-s long, (3840 data points sampled at 128 HZ)

The following parameters were used for both power spectrum and bicoherence estimation:

Segment length (segleng) =3840(30s);

Segment shift overlap (segshift) =segleng/2;

Maximum number of frequency bins (maxfreqbins) =129;

Length of a recording epoch (epleng) =3840 (30 s);

As result analysed frequencies spanned from DC to

60 Hz, with a spectral resolution of 1 Hz

For each frequency pair at the bicoherence matrix B (f1, f2) was obtained according to formula (3) as indicated in the documentation to the METH toolbox.

LBICO Estimation

LBICO was conformed as the sum of a power spectral (LPS) and a bicoherence (LBC) addends.

The LBC addend of a 30-s segment, is defined as:

$$LBC = \frac{\sum_{\Omega_A} B(k_1,k_2)}{\sum_{\Omega_B} B(k_1,k_2)} \quad (4)$$

Where

ΩA ≡ {k1,k2|k1 > 0,k2 > k1,k1 + k2 ∈ [13,60Hz]},

ΩB ≡ {k1,k2|k1 > 0,k2 > k1,k1 + k2 ∈ [9,22Hz]}.

The LPS addend of a 30-s segment, is defined as

$$LPS = \frac{\sum_{\Omega_C} P(k_1,k_2)}{\sum_{\Omega_D} P(k_1,k_2)} \quad (5)$$

Where P(K1,k2) denotes power spectrum, and

ΩC ≡ {k1,k2|k1 > 0,k2 > k1,k1 + k2 ∈ [42,53Hz]},

ΩD ≡ {k1,k2|k1 > 0,k2 > k1,k1 + k2 ∈ [11,13Hz]}.

Finally, the index LBICO is computed as

$$LBICO = 42.957 * (LBC + LPS) + 180 \quad (6)$$

In formula (6), there is no assurance that LBICO values will be bounded by 100, as a final correction, we set equal to 100 those LBICO values exceeding 100. This creates some minor limitations in practical terms, and we hope to subside them in newer versions of the proposed index.

Each subsequent segment was shifted 5 s respect to the preceding one. As result, adjacent LBICO values overlap at 83.33% (25/30), this is a compromise solution for allowing comparison with the BIS™ values on one hand, and having time windows long enough as for making reliable bispectral estimations.

Statistical Analysis

Statistical analysis included time series visualization, linear correlation analysis and Bland-Altman representation of data.

Results

General Description of Data Simultaneously Assessed with LBICO and with BIS™

In figure 2, the LBIS values estimated from an EEG recording are compared to directly measured BIS™ values corresponding to the same5-s intervals. As it can be noticed, there is general agreement between both traces. On the other hand, the large discontinuities in the LBIS trace might be explained by the artifacts in the corresponding EEG trace.

The effect of EEG data quality upon BIS™ can be illustrated with figure 2. As it can be seen, the first half of the EEG trace (bottom panel in the figure) is very irregular, and the LBICO trace is also erratic (top panel). The second half of the same EEG recording is artefact-free and the agreement between LBICO and BIS™ is appreciable.

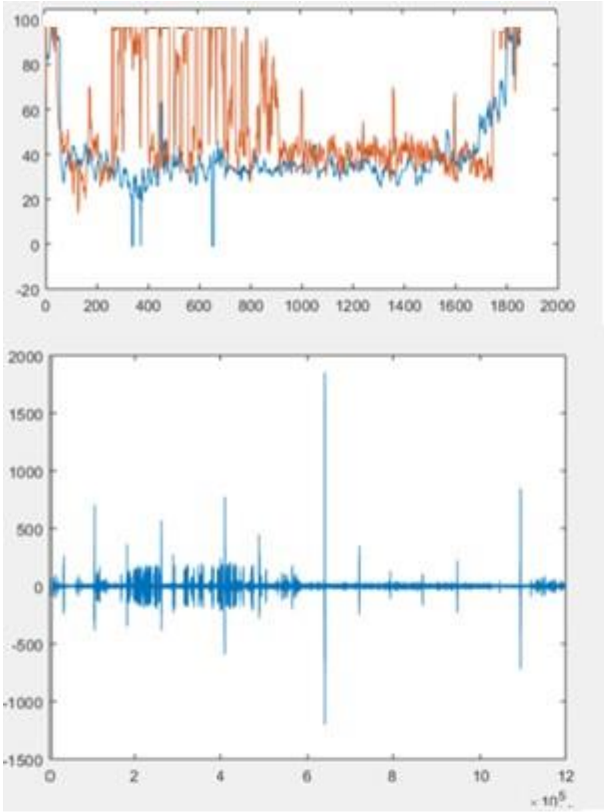

Fig.2- Top: BIS™ values (blue) and estimated LBICO (red) values corresponding to a patient during a surgery in the abscissas axis a value of 1 correspond to 5 s. Bottom: EMD-filtered EEG trace. In the abscissas axis a value of 1 correspond to 7.8 ms. Note that position of EEG artefacts is highly coincident with artefacts in the LBICO continuous line.

In Figure 3, the comparison between LBICO and BIS™ is shown for a recording with a lower number of EEG artefacts. In this case, the coincidence between both indices is apparent.

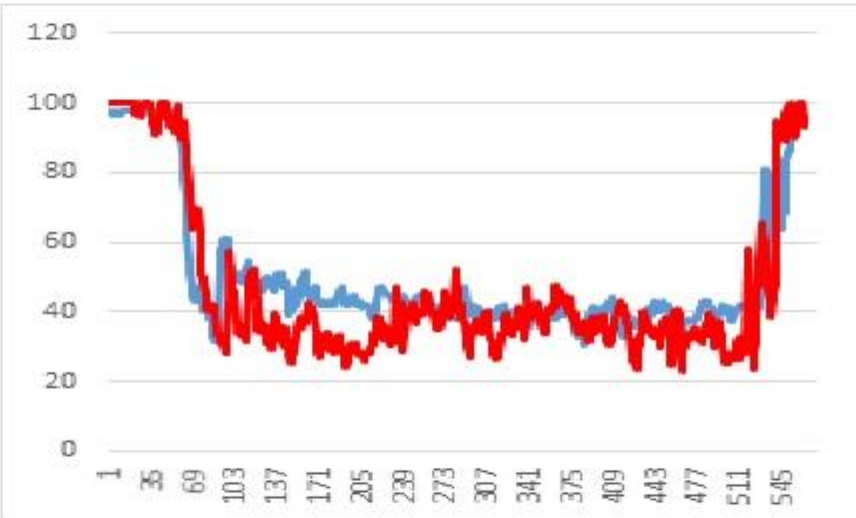

Fig. 3- Data corresponding to other patient. For details, see the top panel of figure 2.

Statistical comparisons between LBICO and BIS™

To numerically assess the correspondence between LBICO and the gold standard, we submitted to analysis a sample of 16861 artefact-free pairs of values taken from all the 24 recordings from the database (corresponding to a total of 23.42 hours of recording).

Results of correlation analysis are summarized in the scatterplot of figure 4. As it can be seen, the slope is close to one (0.93) and the correlation coefficient is 0.70 (p=0.0000), showing good agreement of LBICO with the BIS™ gold standard. This result is further confirmed in the Bland-Altman plot displayed in figure 5.

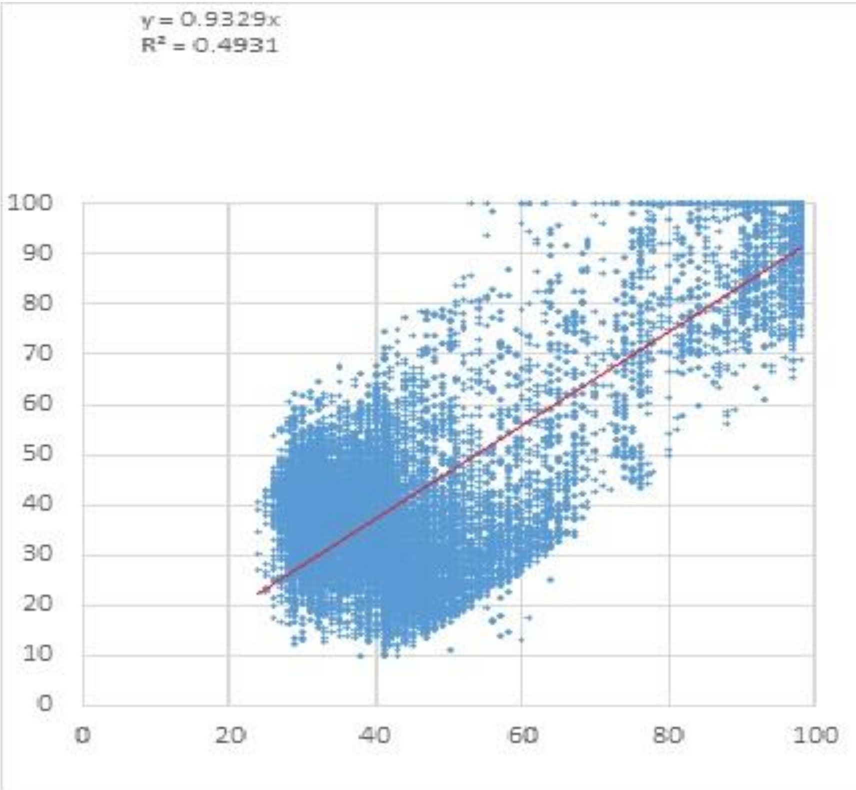

Fig.4- Scatter plot of BIS™ index and LBICO.

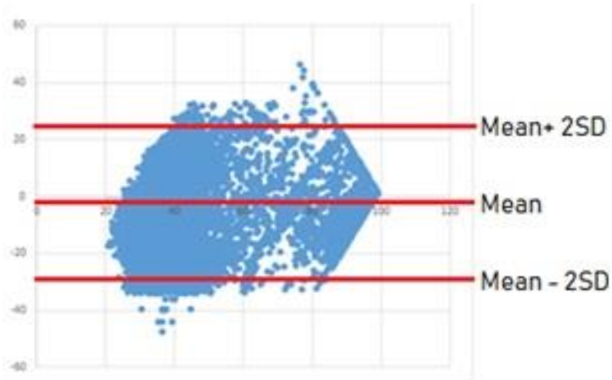

Fig. 5- Bland-Altman Plot of the BIS™ index and the LBICO[27].

Discussion

Our results revealed that the proposed index LBICO performs satisfactorily when compared to the "gold standard" reference given by BIS™.

Salient aspects of LBICO are the inclusion of bicoherence instead of bispectrum (which is customarily used in BIS™), the absence of burst suppression as an addend of the index, and the inclusion of a rather different choice of frequency bands:

ΩA ≡ [13,60Hz]

ΩB ≡ [9,22Hz]

ΩC ≡ [42,53Hz]

ΩD ≡ [11,13Hz]

As it is known, bicoherence is a sensitive means of assessing phase coupling between different frequencies, no matter amplitude differences between involved signals, and this can be in favour of the proposed index. [26-30]

Worth of attention is that frequencies in the delta band were not included into LBICO.

In LBC estimation there is a combination of frequencies covering beta and slow gamma (13-60 Hz) related to EEG activity including theta, alpha and beta bands (9-22 Hz). Different works refer to the importance of theta-gamma phase coupling, especially in the frequencies range of 4-12 Hz for theta and 30-80 Hz. Coupling changes in this region could be detected by summand LBC.[30] Of particular interest is the shift in sleep spindles at 10-18 Hz. In particular, it has been reported an increased correlation of power in the delta and sleep spindle (10–18 Hz) bands with hippocampal ripples.[31-33]

It has been also reported that the administration of small doses of a GABAA hypnotic induces sedation. If the dose is increased slowly, the patient can enter a state of paradoxical excitation or disinhibition defined by euphoria or dysphoria, incoherent speech, purposeless or defensive movements, and increased electroencephalogram (EEG) oscillations in the beta range (13–25 Hz).[33]

Also interesting is that the LPS component, related to power spectrum changes in beta (11-13 Hz) and gamma 42-53 Hz bands, is related to a frequency region where important changes do occur during sleep, sedation and anaesthesia.

Limitations of present study

The first limitation of this study is related to the database used. It contains a rather limited number of cases (N=24) and many of the EEG recordings were contaminated with artifacts. The use of a more comprehensive database would be of greater help. The approach used to correct artifacts through EMD, even when correcting an important part of them, is still limited, and a further research is needed to propose a more parsimonious approach to artifact correction.

The second limitation is related to the lack of information about clinical assessment of DoA as well as of blood concentration of anaesthetic substances. Given the limitations of BIS™ on this aspect, lacking this information could affect the performance of LBICO. Further research by our group considers the continuous recording of LBICO in the surgery theatre.

Thirdly, we did not observe burst suppression events in these EEG recordings, and there remains as a doubt how their presence could affect the diagnostic precision of LBICO, as well as the way their incorporation into formula (6) could affect LBICO correspondence to the BIS™ gold standard.

Conclusions

This study was related to the search of a Bicoherence based index to assess DoA. Our results showed that a substantial narrowing in the frequencies of interest selection allowed yielding satisfactory results when compared to the BIS™ gold standard. We expect that the index may be further perfection mainly through inclusion of additional EEG channels as well as via recording electrocardiogram and photoplethysmographic signals, an option that is non invasive and potentially very informative.

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Conflicts of Interests

None to declare

Author Contributions

Dr. C. José Luis Hernandez-Cáceres: contributed to the research design and discussion of the analysis strategies and wrote the manuscript. Dra. C. Lourdes Diaz-Comas, Lic. José Manuel Antelo-Cordovés, Dra. C. Marlis Ontivero-Ortega, Lic. Ronaldo Cesar Garcia-Reyes, Dra. C. Lidia Charroó-Ruiz, Dra. C. Ana Calzada-Reyes: contributed to analysis strategies and wrote the manuscript. All authors contributed to the article and approved the submitted version.