Review Article *Open Access*

Journal of Advanced Clinical Neurology Research

ISSN: 3071-0731

DOI: doi.org/10.63721/26JACNR0121

Novel Reduction on Serum Homocysteine and Creatinine Level After Intravascular Laser Irradiation of Blood: A Ten -Year Retrospective Cohort

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Citation: *Shin-Tsu Chang, VGHKS Phototherapy Investigators Group (2026) Novel Reduction on Serum Homocysteine and Creatinine Level After Intravascular Laser Irradiation of Blood: A Ten -Year Retrospective Cohort. J. of Adv Clin Neu Res 2(2), 01-09. WMJ/JACNR-121*

Abstract

Laser-based therapy may contribute to maintaining hemodynamic equilibrium in affected individuals. The present study was designed to evaluate the levels of the biomarkers homocysteine and creatinine following the clinical application of intravascular laser irradiation of blood (iLIB). We further investigated whether iLIB could improve hematological parameters and examined medication usage before and after iLIB intervention.

Methods: *Patients who consecutively underwent iLIB treatment from January 2013 through December 2022 were included for analysis. A retrospective evaluation was conducted to determine the relationship between laboratory findings and iLIB therapy. Clinical characteristics and blood parameters were compared within three months prior to the initial treatment and three months following the final treatment session. Additionally, we analyzed pre- and post-treatment changes between patients receiving 1–9 sessions (Group 1) and those receiving ≥ 10 sessions (Group 1) of iLIB therapy.*

Results: *A total of 538 eligible individuals who underwent iLIB treatment were analyzed. Following therapy, both homocysteine and creatinine levels showed significant reductions in each group (all $p < 0.001$). Furthermore, statistically significant differences between the groups were observed ($p < 0.05$) for both homocysteine and creatinine.*

Conclusions: *iLIB therapy appears to be an effective, advantageous, and practical intervention for reducing homocysteine and creatinine levels. The findings of this study suggest that reductions in these biomarkers after iLIB treatment may be indicative of improvements in cardiovascular dysfunction among treated patients.*

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Submitted: 05.04.2026 **Accepted**: 10.04.2026 **Published**: 23.04.2026

Keywords: Intravascular Laser Irradiation of Blood, Balance, Hyperhomocysteinemia, Statins, Chronic Kidney Disease, Aerobic and Anaerobic, Nitric Oxide, Adenosine Triphosphate

Introduction

Homocysteine is a sulfur-containing amino acid generated during the metabolism of dietary methionine and is widely recognized as a risk factor for atherothrombotic vascular disorders. Over recent decades, homocysteine has been regarded globally as an important biomarker associated with vascular disease [1]. Accumulating evidence indicates that patients presenting with acute stroke in combination with hyperhomocysteinemia have a heightened risk of early neurological decline [2], and elevated homocysteine levels have been shown to adversely affect vascular endothelial cell function in human studies [3]. Increased homocysteine concentrations are also associated with a higher likelihood of recurrent ischemic stroke during the recovery phase following an acute stroke event [4].

Creatinine serves as a key indicator of renal function, and precise measurement is crucial for estimating glomerular filtration rate, which plays a central role in the diagnosis, staging, and management of chronic kidney disease (CKD) [5]. Therefore, identifying effective strategies to reduce homocysteine and creatinine levels remains an important objective in clinical practice.

Intravascular photobiomodulation (iLIB) has been utilized since the 1960s; this non-pharmacological modality was initially applied in the management of cardiovascular diseases and is thought to enhance both blood circulation and cellular blood function [6]. iLIB is considered a safe and beneficial laser-based therapeutic approach [7], and it is currently employed as an adjunctive treatment for pain control in conditions such as diabetic neuropathy, fibromyalgia, arthritis [8-10]. And some immune disordersMoreover, iLIB has demonstrated substantial efficacy in treating vascular disorders, cardiac conditions, tissue repair processes, and various pathological states , particularly in CKD [11-15]. Previous investigations have also reported the effects of laser therapy on a range of hematological biomarkers in conditions including diabetes and hypercholesterolemia [16,17]. In the present study, homocysteine was selected as a biomarker due to its recognized role in predicting cardiovascular complications [18-20].

Homocysteine as a stroke-related risk factor has not yet been clearly addressed in the context of pre- and post-iLIB treatment within the existing literature [21]. Similarly, despite homocysteine being well established as a stroke risk factor, there remains a lack of studies evaluating its levels before and after iLIB intervention [21]. Two previously published case reports involving stroke patients—both hemorrhagic and ischemic types—treated with iLIB demonstrated normalization of homocysteine levels, where serum homocysteine concentrations were assessed before and after therapy, and the authors concluded that iLIB may exert dual effects by enhancing thalamic perfusion while simultaneously promoting homocysteine metabolism [22,23].

Based on these observations, we hypothesize that iLIB may reduce homocysteine and creatinine levels through metabolic modulation. Accordingly, we performed a controlled analysis comparing blood parameters before and after iLIB therapy in patients. In addition, we compared outcomes between patients receiving 10 sessions and those receiving 1–9 sessions of iLIB to determine whether a higher treatment frequency confers greater therapeutic benefit.

Methods

Participants

This investigation was designed as a single-center retrospective study conducted in Taiwan. The study protocol received approval from the Committee on

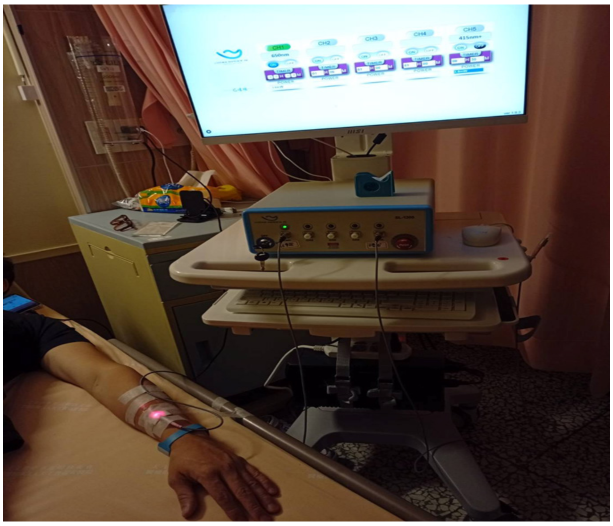
Human Research at Kaohsiung Veterans General Hospital (IRB number: KSVGH20-CT-16), and the requirement for informed consent was waived due to the retrospective nature of the study and the minimal risk posed to participants. All collected data were anonymized, ensuring that no personal identifiers or names were disclosed. We retrospectively accessed the KSVGH database to extract information on all patients who had undergone iLIB therapy.

Eligibility for inclusion was defined by receipt of iLIB treatment identified through specific charge codes (66026C, 66029J, 66039, and 66040). All iLIB procedures were carried out by experienced physiatrists. Patients lacking complete data for the three months preceding the initial iLIB session or the three months following the final session were excluded from the analysis.

Intervention of iLIB

We utilized a laser illumination system manufactured by "Liverage" (Multi-wavelength Laser treatment instrument SL-1200, LIVERAGE BIOMEDICAL INC., Taiwan)

Figure1: Laser Devise and its application in one patient



This device was equipped with dual wavelengths: 415 nm (blue light, energy ranging from 15.12 to 16.56 J, energy density from 12096 to 13248 J/cm2, power output between 3.36–3.68 w/cm2, and power intensity from 2.285–2.502 w/cm2) and 650 nm (red light, energy ranging from 13.68 to 15.12 J, energy density from 10944 to 12096 J/cm2, power output between 3.04–3.36 w/cm2, and power intensity from 2.128–2.352 w/cm2). A trained nurse connected the Optical Fiber Needle ("Liverage" Multi-wavelength Laser Treatment Instrument Accessories, GA-024) to the venipuncture site and initiated simultaneous exposure to both red and blue light at equal intensity and duration. The applied intensity ranged from 3–5 mW, with an energy density of 22.86 J/cm2 for both wavelengths. Each treatment session lasted a total of 60 minutes, with equal time allocated to each wavelength.The iLIB therapy was delivered as a single treatment course over two consecutive weeks on weekdays. Multiple treatment courses were separated by rest intervals ranging from one to three weeks, spanning a total treatment duration of two to three months. The procedure involved inserting an optical fiber with a diameter of 0.5 mm through a phlebotomy cannula into an accessible peripheral vein. This method allowed nearly 100% of the total circulating blood volume to be exposed to laser irradiation during each 60-minute session. Although iLIB requires venous catheter insertion, it is generally regarded as minimally invasive, as it does not involve surgical incisions or major operative procedures. Nonetheless, catheter placement may cause mild discomfort and carries potential risks, including bleeding, infection, or venous inflammation.

In summary, iLIB represents a minimally invasive therapeutic technique that utilizes low-level laser irradiation to activate cellular processes and enhance systemic blood circulation. The procedure is administered via a venous catheter, enabling irradiation of nearly the entire blood volume during each treatment session.

Data Collection

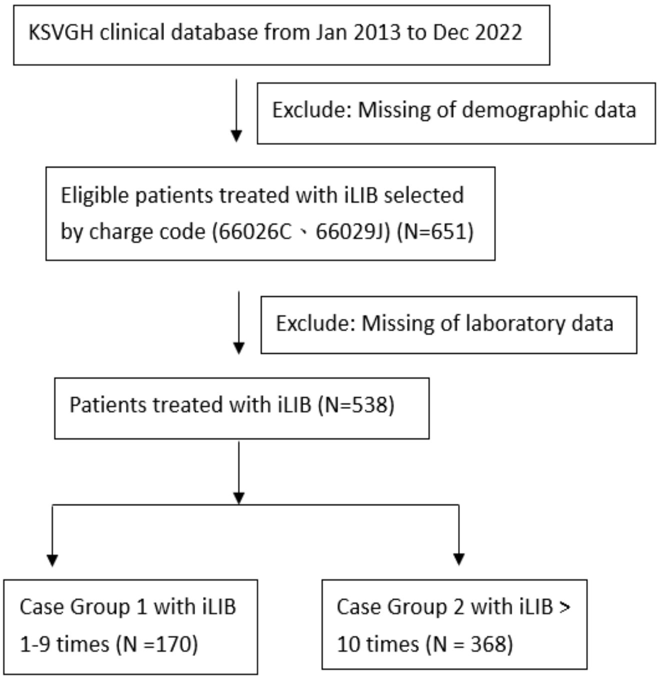
All study data were retrospectively obtained from medical records, including demographic information and laboratory parameters. Patient characteristics and blood test results were compared within the three months preceding the first iLIB session and the three months following the final session. Additionally, pre- and post-treatment laboratory data were analyzed between patient groups (Group 1 and Group 2). The evaluated biochemical variables included creatinine and serum homocysteine levels.

Statistical Analysis

Baseline demographic and clinical characteristics were summarized for the overall study population and stratified into two groups based on treatment frequency: 1–9 iLIB sessions (Group 1) and ≥ 10 sessions (Group 2). These data were presented as mean ± standard deviation for continuous variables or as counts with percentages for categorical variables. For continuous variables, comparisons between iLIB-treated and non-treated groups were conducted using independent samples t-tests or one-way analysis of variance (ANOVA). Comparisons of measurements before and after iLIB therapy were performed using paired samples t-tests or the Wilcoxon rank-sum test. For categorical variables, intergroup comparisons were conducted using the Chi-squared test or Fisher's exact test when expected cell counts were less than 5. All statistical analyses were carried out using Statistical Analysis Software (SAS; version 9.4; SAS System for Windows) and SPSS (version 20; SPSS Inc., Chicago, IL, USA). A p value of <0.05 was considered indicative of statistical significance.

Results

The subjects and study cohorts were selected according to the process presented in Figure 2. Flow chart



A total of 651 patients who received iLIB therapy between January 2013 and December 2022 were evaluated. We excluded 113 patients whose clinical profiles were not available or had missing data. Of 538 patients aged 25 to 75 years old (284 males, 254 females; mean age, 60.8 ± 14.9) met the selection criteria and were enrolled in this study. We classified these 538 patients into two groups according to their number of iLIB treatments: 170 patients as Group 1 and the other 368 patients as Group 2. All patients were records having pain, at least one, in any part of their body.

Table 1: presents the baseline demographic characteristics of the total 538 patients with iLIB during 2013/1 to 2022/12., and Table 2 summarizes the blood parameters.

Variable	Total n=538 (%)
Age, years (Mean±SD) Gender-Male Comorbidity-Yes	59.9±14.0 284 (52.8)
HTN	130 (24.2)
DM	62 (11.5)
Hyperlipidema	100 (18.6)
CKD	20 (3.7)
CAD	42 (7.8)
HF	9 (1.7)
COPD	11 (2.0)
Chronic liver disease	15 (2.8)
Stroke	117 (21.7)

* : p<0.05

Table 2: Comparison of the lab data between the before and after iPBM.

Variable	Groups	before	after	P-value
Hcy	Group 1	17.6 ±38.4	14.2±13.3	<0.001
	Group 2	18.5±51.0	13.8±10.8	<0.001
Cr	Group 1	1.7±0.7	0.8±0.3	<0.001
	Group 2	2.1±2.1	1.6±2.7	<0.001

As shown in Table 2, homocysteine and creatinine decreased significantly after treatment in both groups. The homocysteine levels decreased from 17.6 to 14.2 and 18.5 to 13.8 in both groups, respectively ($p < 0.001$). The creatine levels decreased from 1.7 to 0.8 and 2.1 to 1.6 in both groups, respectively ($p < 0.001$). In the comparison of the difference of post-treatment values of Group 1 and Group 2, homocysteine ($p = 0.014$) and Cr ($p = 0.003$) were significantly higher in the patients in both groups.

Discussion

The results of this investigation demonstrated that, among the 538 participants, both homocysteine and creatinine levels showed a mean reduction following iLIB administration, regardless of whether individuals received 1–9 sessions (Group 1) or ≥ 10 sessions (Group 2). The homocysteine concentrations declined from 17.6 to 14.2 in Group 1 and from 18.5 to 13.8 in Group 2 ($p < 0.001$). Likewise, creatinine values decreased from 1.7 to 0.8 in Group 1 and from 2.1 to 1.6 in Group 2 ($p < 0.001$). These findings imply that iLIB therapy may serve as a potentially effective approach for lowering both homocysteine and creatinine concentrations.

Photobiomodulation has gradually superseded the earlier terminology of low-level laser therapy, as the latter inadequately reflects the roles of electrical and total energy dynamics. This modality functions as a light-based treatment utilizing nonionizing light sources to induce non-thermal biological effects, whereby endogenous chromophores trigger photophysical and photochemical cascades across multiple biological layers [24,25]. Prior studies suggest that iLIB may exert beneficial effects across various organ systems through immune modulation, enhancement of oxygen transport capacity in blood cells, and augmentation of circulation [26,27]. In addition, low-power laser exposure may improve red blood cell oxygenation as well as deformability, thereby potentially facilitating tissue regeneration and alleviating pain [28,29]. Certain investigations have reported that iLIB can partially influence red blood cell counts in smaller sample populations [30,31]. Furthermore, reductions in homocysteine levels following iLIB therapy have also been observed in patients undergoing mastectomy [32,33]. Notably, our findings align with earlier research that evaluated iLIB interventions across diverse clinical scenarios [13,16,17,32-36]. Regarding the potential mechanisms by which iLIB contributes to reductions in serum homocysteine and creatinine, several plausible explanations can be proposed. First, iLIB has been shown to enhance adenosine triphosphate (ATP) generation and optimize mitochondrial activity within cells, which may help mitigate oxidative stress and inflammatory responses as documented in certain studies [34,37,38]. The enhancement of intracellular ATP synthesis is considered a key factor underlying the observed reduction in creatinine levels following iLIB treatment [37]. This improvement in cellular energy status appears to be closely associated with increased oxidative metabolic activity. A comprehensive review has indicated that iLIB demonstrates beneficial effects in both animal experiments and human clinical studies [39].Second, iLIB appears to facilitate coordination between aerobic and anaerobic pathways of ATP production [40]. Irrespective of the dominant metabolic pathway, diminished ATP production due to mitochondrial dysfunction can compromise overall cellular performance [41]. Consequently, by restoring mitochondrial efficiency—such as enhancing energy output and modulating redox balance—iLIB may improve organ function, particularly renal performance, thereby contributing to decreased creatinine levels [19].

Third, evidence suggests that iLIB therapy can promote nitric oxide production, a powerful vasodilator that enhances blood circulation and tissue oxygen delivery [43, 44]. The resulting improvements in perfusion and oxygenation may support cellular metabolism while reducing inflammatory processes, ultimately contributing to lower creatinine concentrations. Moreover, iLIB may directly influence mitochondrial activity, thereby enhancing cellular energy production and metabolic efficiency, which further supports reductions in creatinine [37]. Laser irradiation may also stimulate nitric oxide synthesis, a key signaling molecule involved in vascular tone regulation, thereby improving circulation and oxygen transport, which may contribute to lowering both homocysteine and creatinine levels [43]. Through nitric oxide induction and modulation of inflammatory signaling pathways, iLIB may help establish a more balanced physiological state, potentially decreasing cardiovascular risk and improving clinical outcomes in mastectomized patients as well as in neurological disorders [32,33,45-48]. Additionally, iLIB has been reported to enhance regional blood flow and oxygenation, thereby facilitating tissue repair and attenuating inflammation [49]. These observations highlight the need for further studies to better elucidate the role of iLIB in hemodynamic regulation.

Fourth, iLIB appears to play a critical role in modulating mitochondrial respiratory function under conditions of oxidative stress [50]. In patients with CKD, significant dysregulation of mitochondrial respiratory processes has been closely linked to elevated oxidative stress, wherein increased production of reactive oxygen species driven by pro-inflammatory mediators may suppress oxidative phosphorylation and trigger compensatory intracellular oxidative responses [51]. Using CKD as an illustrative example, it is hypothesized that patients in a state of severe electrochemical imbalance may respond to even a single iLIB intervention with biochemical changes sufficient to reduce creatinine levels.

This study is subject to several inherent limitations. First, as a retrospective analysis, certain key variables were either unavailable or incomplete, including some pre- and post-treatment measurements. Second, the study did not include a control group for comparison. Nevertheless, it should be emphasized that the study was intentionally designed as an exploratory assessment of therapeutic potential, and the absence of a control group was a deliberate choice to enhance feasibility and increase sample size. Future research will aim to incorporate controlled study designs to further clarify therapeutic effects and underlying mechanisms. Third, a meta-analysis has indicated that statin therapy, commonly used for secondary stroke prevention, may also reduce homocysteine levels, thereby complicating the isolation of iLIB-specific effects. Finally, as the study population consisted exclusively of patients from Taiwan, additional investigations are required to determine whether similar outcomes can be observed in other Asian and Western populations[52].

Conclusions

In conclusion, the present cohort supports that iLIB therapy represents an effective, beneficial, and practical intervention for reducing homocysteine and creatinine levels over both short-term and long-term periods. The observed decreases in these biomarkers suggest meaningful improvements in the function of critical organs, particularly reflecting enhanced interplay between cardiovascular and renal systems, and indicating a potential systemic health benefit associated with iLIB therapy.

Funding: This research received no external funding.

Institutional Review Board Statement: The study design was approved by Kaohsiung Veterans General Hospital Committee on Human Research (IRB number: KSVGH20-CT-16).

Informed Consent Statement: The requirement for informed consent was waived due to the retrospective study design and minimal risk to participants.

Data Availability Statement: All data were deidentified, and no names or identifying information were revealed.

Conflicts of Interest: The authors declare no conflict of interest.

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