LABORATOIRE SION
BIOLOGICAL ANALYSIS AND MEDICAL IMAGING
Specialized tests – Ultrasound – specimen collection at home or at the office.

ISCHEMIA-MODIFIED ALBUMIN (IMA)

Monday 11 May
2026

Abstract

Ischemia-modified albumin (IMA) is an early biomarker of ischemic events, detectable as soon as 6 to 10 minutes after the onset of ischemia and persisting for approximately 12 hours. Its measurement by the albumin cobalt binding (ACB) test is approved by the United States Food and Drug Administration (FDA). In the African and Cameroonian context, marked by a high prevalence of cardiovascular diseases, limited access to advanced imaging techniques and frequent late presentation of patients, IMA represents a rapid, inexpensive diagnostic tool that complements the standard cardiac work-up, particularly in the triage of chest pain in the emergency department.

Introduction

Cardiovascular diseases are the leading cause of death in many sub-Saharan African countries, accounting for up to 40 % of deaths in some populations. In Cameroon, ischemic heart disease is steadily increasing, driven by rapid urbanization, sedentary lifestyles, the growing prevalence of type 2 diabetes and arterial hypertension, as well as by unfavourable dietary habits. This epidemiological transition places acute coronary syndromes (ACS) among the most frequent and most lethal medical emergencies in our health facilities.

Early diagnosis of myocardial ischemia remains a major challenge. Conventional tools such as the electrocardiogram (ECG), cardiac troponin measurement and echocardiography are not always available in a timely manner. Moreover, troponin, although the reference biomarker of myocardial necrosis, rises only after several hours of prolonged ischemia. As a result, a critical therapeutic window is often missed in our hospitals.

It is in this context that ischemia-modified albumin (IMA, Ischemia Modified Albumin) is attracting growing interest. This biomarker, detectable within the very first minutes of an ischemic episode, offers a unique opportunity for the early identification of at-risk patients. The present review examines the biochemical basis, the assay methods and the clinical value of IMA, placing them in the context of medical practice in Africa and in Cameroon.

2. PATHOPHYSIOLOGY

2.1. Formation of IMA

Human serum albumin (HSA) is the most abundant plasma protein (60 % of plasma proteins) and is synthesized by the liver. Its N-terminal region (sequence Asp-Ala-His-Lys) constitutes a preferential binding site for transition metals, in particular cobalt (Co^{2}), copper (Cu^{2}) and nickel (Ni^{2}), owing to its square-planar geometry (Figure 1). During an ischemic episode, several mechanisms converge to irreversibly modify this N-terminal region:

- The local acidosis generated by anaerobic glycolysis releases Cu^{2} ions from their weak binding sites on plasma proteins.
- These Cu^{2} ions are reduced to Cu by reducing agents (ascorbic acid), then re-oxidized, generating superoxide radicals (O2•).
- Through the Fenton reaction (in the presence of Cu^{2}/Fe^{3}), hydrogen peroxide generates hydroxyl radicals (•OH), which are extremely reactive.
- These free radicals specifically damage the N-terminal site of HSA, causing the loss or the modification of two to four terminal amino acids, which abolishes the metal-binding capacity.

The albumin thus modified constitutes IMA. Its serum level rises within 6 to 10 minutes after the onset of ischemia and remains elevated for approximately 12 hours before gradually returning to normal. This rapid kinetic profile contrasts with that of troponin, which rises only after 3 to 6 hours and reflects an already established myocardial necrosis.

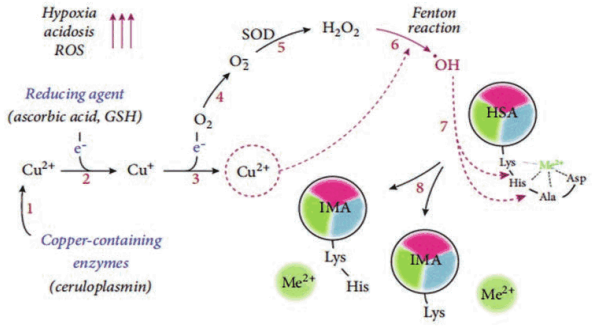

Figure 1: Mechanism of formation of IMA induced by oxidative stress.

Tissue hypoxia and the activation of anaerobic glycolysis cause acidosis and lead to the release of Cu^{2+} ions by copper-containing proteins, such as ceruloplasmin (1). In the presence of reducing agents, for example ascorbic acid, Cu2+ is reduced to Cu+ (2), which leads to the formation of the superoxide anion O2− (3-4). Superoxide dismutase (SOD) catalyses the dismutation of superoxide O2− into hydrogen peroxide H2O2 (5) which, in the presence of Cu^{2}, undergoes the Fenton reaction with formation of hydroxyl radicals ·OH (6). These radicals contribute to the degradation of the N-terminal sequence (7) and to the formation of IMA (8), which cannot bind Cu2+ or other metal ions.

3. SAMPLE COLLECTION

3.1. Tube type and nature of the specimen

IMA is measured on serum. The tube to be used is the plain tube (red or yellow cap, without anticoagulant) or the gel separator tube. EDTA (purple tube) and the other anticoagulants must be avoided, because they chelate metal ions and directly interfere with the ACB test by altering the availability of cobalt in the sample.

3.2. Timing of sample collection

The time of collection is a determining factor for the interpretation of the result. Given the particular kinetics of IMA, the following recommendations apply:

- Collection on admission to the emergency department: ideally within the 30 minutes following the arrival of the patient with chest pain. IMA is already detectable as early as 6 to 10 minutes after the onset of ischemia.
- Simultaneous troponin + IMA collection: the combination is recommended from admission onwards. If both are negative, the short-term ischemic risk is very low (NPV > 90 %).
- Control sample at H3–H6: useful if the first sample was taken early and if the clinical picture remains suspicious. Troponin rises within this time frame, allowing confirmation.
- Do not sample after 12 hours of ischemic evolution for IMA: the level returns spontaneously to baseline values, which may give a false negative.

4. ASSAY METHODS

4.1. Albumin cobalt binding (ACB) test

The ACB (Albumin Cobalt Binding) test, introduced by Bar-Or et al. in 2000, is the reference method approved by the United States Food and Drug Administration (FDA). Its principle rests on the reduction of the capacity of albumin to bind exogenous cobalt (see Figure 1 above). It is automatable and adaptable to the standard biochemistry analysers available in our health facilities.

4.2. Comparison of the available methods

Method	Principle	Advantages / Limitations
ACB (cobalt)	Cobalt–albumin binding, colorimetry at 470 nm	Rapid, inexpensive, automatable; moderate specificity
ACuB (copper)	Copper–albumin binding, fluorescence (Lucifer Yellow)	Increased sensitivity; specialized equipment required
IMA ELISA	Antibodies directed against modified N-terminal albumin	Quantitative, high specificity; lengthy procedure
SPR immunosensor	Surface plasmon resonance + gold nanoparticles	Very low LOD (10 ng/L); expensive
Q-XRF	X-ray fluorescence coupled with quantum dots	Specificity 95.9 %; highly specialized equipment

For the African context, the ACB test remains the most suitable method: moderate cost, short turnaround time, and the possibility of integrating it into existing workflows. It is recommended to report the result relative to the serum albumin level (IMA/Alb ratio in U/g) in order to overcome the variations in albumin concentration that are frequent in undernourished patients or in patients with chronic diseases.

5. REFERENCE VALUES AND INTERPRETATION

Parameter	Indicative threshold	Interpretation
IMA (U/mL)	> 85	Probable ischemia range
IMA (U/mL)	0-78	Normal

6. COMBINED STRATEGY: IMA + TROPONIN + ECG

IMA should not replace but complement the standard cardiac work-up. Its combination with troponin (even conventional troponin) and with the ECG significantly improves early diagnostic sensitivity. In a patient presenting with typical chest pain with a non-contributory ECG and a normal troponin on admission, a negative IMA makes it possible to point towards a non-ischemic diagnosis with a high degree of confidence, thereby reducing unnecessary hospital admissions and optimizing the allocation of resources. Conversely, an elevated IMA in the presence of a still normal troponin should alert the clinician and prompt close monitoring.

7. LIMITATIONS AND PERSPECTIVES

IMA is not exclusively cardiac. Any state of tissue ischemia, hypoxia, acidosis or oxidative stress can raise its level. This gives IMA a high sensitivity but a relative specificity, which requires its interpretation within a rigorous clinical and laboratory context.

Moreover, the absence of specific African reference values calls for caution in the interpretation of published thresholds. Many conditions that are common in Cameroon (severe malaria, sickle cell disease, malnutrition with hypoalbuminaemia, chronic infections) can alter the albumin level and potentially interfere with the assay. Adjusting the result to the serum albumin level partially attenuates these interferences.

Local cohort studies, conducted in the emergency departments of Douala, Yaoundé and secondary cities, are necessary in order to establish Cameroonian reference values.

Conclusion

Ischemia-modified albumin (IMA) represents a genuine diagnostic advance in the early management of ischemic syndromes. Its profile (early rise, technical accessibility, moderate cost and good negative predictive value) makes it a biomarker particularly well suited to the requirements and the constraints of the health systems of sub-Saharan Africa.

For the physician confronted with chest pain in an emergency setting, IMA constitutes a valuable complementary tool. A negative result helps to rule out acute ischemia; a positive result strengthens the indication for close monitoring and for urgent cardiological management. The combination IMA + troponin + ECG thus represents a synergistic diagnostic strategy, feasible in the majority of our health facilities. Rigorous sample collection (serum, timing adapted to the window of positivity, and IMA/Alb ratio) remains the sine qua non condition of a reliable interpretation.

References

1. Senadeera NN, Ranaweera CB, Perera IC, Kottahachchi DU. Biochemical Insights and Clinical Applications of Ischemia-Modified Albumin in Ischemic Conditions. J Vasc Dis. 2024;3:245-266.

2. Sinha MK, Gaze DC, Tippins JR, Collinson PO, Kaski JC. Ischemia Modified Albumin Is a Sensitive Marker of Myocardial Ischemia After Percutaneous Coronary Intervention. Circulation. 2003;107:2403-2405.

3. Lagabrielle JF, Delarche N, Adamou TH, Fabre E. Dosage de l'albumine modifiée par l'ischémie (IMA) dans le cadre d'angioplasties programmées. Immuno-analyse Biol Spécialisée. 2005;20:221-227.

4. Demirtas AO, Karabag T, Demirtas D. Ischemic Modified Albumin Predicts Critical Coronary Artery Disease in Unstable Angina Pectoris and Non-ST-Elevation Myocardial Infarction. J Clin Med Res. 2018;10(7):570-575.

5. Kabadayi Sahin E, Turan G, Neselioglu S, Atagun MI. Ischemia modified albumin: A potential marker for global metabolic risk in generalized anxiety disorder and panic disorder. Turkish J Clinical Psychiatry. 2021;24:153-159.

6. Bar-Or D, Lau E, Winkler JV. A novel assay for cobalt-albumin binding and its potential as a marker for myocardial ischemia. J Emerg Med. 2000;19:311-315.

7. Christenson RH, Duh SH, Sanhai WR, et al. Characteristics of an Albumin Cobalt Binding Test for Assessment of Acute Coronary Syndrome Patients: A Multicenter Study. Clin Chem. 2001;47:464-470.

8. Peacock F, Morris DL, Anwaruddin S, et al. Meta-analysis of ischemia-modified albumin to rule out acute coronary syndromes in the emergency department. Am Heart J. 2006;152:253-262.

9. Shevtsova A, Gordiienko I, Tkachenko V, Ushakova G. Ischemia-Modified Albumin: Origins and Clinical Implications. Dis Markers. 2021;2021:9945424.

10. World Heart Federation. World Heart Report 2023. Geneva: WHF; 2023.

Contact: 6 99 74 92 47 / 6 76 16 33 53 / 672 26 63 86; Email: contact@laboratoiresion.org