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Coagulation Dynamics Post Cardio-pulmonary Resuscitation.

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Abstract: *Cardiopulmonary resuscitation (CPR) is a series of life-saving actions that improve the chances of survival, following cardiac arrest. Cardio- pulmonary resuscitation is a war against death and return of spontaneous circulation (ROSC) is the victory, but what if someone told that there is lot of battle left ahead. This study aims at discussing the post war scenario which is coagulation changes in body after post Cardio-pulmonary resuscitation. Derangements in the coagulation and fibrinolytic systems changes play a significant role in the spectrum of conditions classified as "post–cardiac arrest syndrome(PACS). The aim of this study is to sensitize the health care system about the change in the coagulation profile in post CPR and its effect in outcome of CPR in terms of survival of the patients.*

Keywords: *Cardiopulmonary resuscitation (CPR), Return of spontaneous circulation (ROSC), Fibrinolytic, Post –cardiac arrest syndrome(PACS).*

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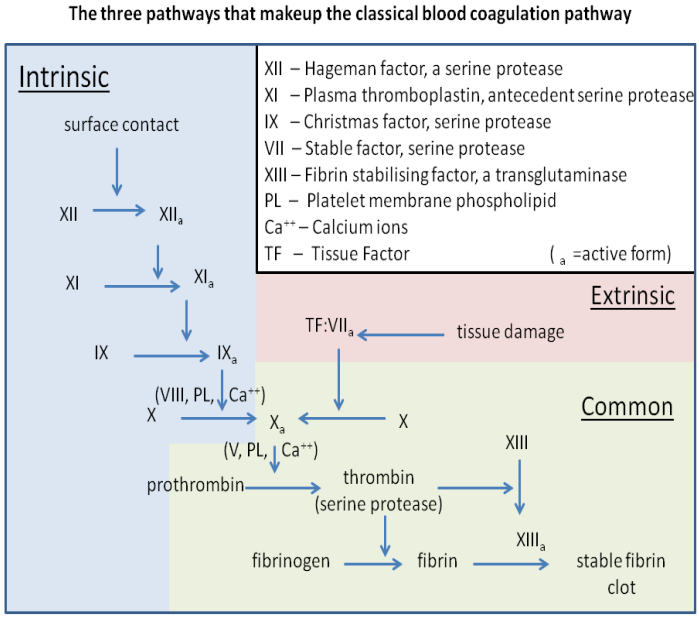
I. Introduction

Cardiopulmonary resuscitation (CPR) is a series of life-saving actions that improve the chances of survival, following cardiac arrest. Successful resuscitation, following cardiac arrest, requires an integrated set of coordinated actions represented by the links in the Chain of Survival. The links include the following: immediate recognition of cardiac arrest and activation of the emergency response system, early CPR with an emphasis on chest compressions, rapid defibrillation, effective advanced life support, and integrated post-cardiac arrest care. The newest development in the CPR guideline is a change in the basic life support sequence of steps from "A-B-C" (Airway, Breathing, Chest compressions) to "C-A-B" (Chest compressions, Airway, Breathing) for adults. Also, "Hands-Only (compression only) CPR" is emphasized for the untrained lay rescuer. On the basis of the strength of the available evidence, there was unanimous support for continuous emphasis on high-quality CPR with compressions of adequate rate and depth, which allows for complete chest recoil, minimizing interruptions in chest compressions and avoiding excessive ventilation. High-quality CPR is the cornerstone of a system of care that can optimize outcomes beyond return of spontaneous circulation (ROSC). There is an increased emphasis on physiologic monitoring to optimize CPR quality, and to detect ROSC(1). Cardio- pulmonary resuscitation is a war against death and return of spontaneous circulation (ROSC) is the victory, but what if someone told that there is lot of battle left ahead. This study aims at discussing the post war scenario which is coagulation changes in body after post Cardio-pulmonary resuscitation. Derangements in the coagulation and fibrinolytic systems changes play a significant role in the spectrum of conditions classified as "post–cardiac arrest syndrome."(2) It consists of four syndromes including systemic ischemia/reperfusion responses and post-cardiac arrest brain injury.

The major pathophysiologies underlying systemic ischemia/reperfusion responses are systemic inflammatory response syndrome and increased coagulation, leading to disseminated intravascular coagulation (DIC), which clinically manifests as obstruction of microcirculation and multiple organ dysfunctions. In particular, thrombotic occlusion in the brain due to DIC, referred to as the "no-reflow phenomenon," may be deeply involved in post-cardiac arrest brain injury, which is the leading cause of mortality in patients with PCAS.

Whole-body ischemia/reperfusion due to cardiac arrest and subsequent ROSC can produce SIRS, which is characterized by the release of systemic pro-inflammatory cytokines and generalized activation of leukocytes and endothelial cells. Recent advances in immunology have elucidated the involvement of innate immunity for the process of SIRS(3). Damage-associated molecular patterns (DAMPs), which are molecules derived from stressed or damaged cells and tissues, are sensed by pattern-recognition receptors expressed on immune cells and endothelial cells. These sensed signals lead to the production of pro-inflammatory cytokines, which stimulates the production of inflammatory biomarkers(4).

Patients with PCAS are in a condition of hypercoagulation, as has been confirmed by previous studies showing increased levels of soluble fibrin (5, 6), fibrinopeptide A (7), tissue factor antigen (8), and thrombin–antithrombin complex (9). Ischemia (hypoxia)/reperfusion due to cardiac arrest and ROSC and subsequent excessive catecholamine release due to shock-induced sympathoadrenal activation cause endothelial activation and injury. These changes induce the expression of tissue factor on the endothelial cells (10). Tissue factor exposed in the circulating blood binds to activated factor VII (FVIIa) (formerly known as the "extrinsic coagulation pathway").



Coagulofibrinolytic changes in patients with PCAS are characterized by tissue factor-dependent coagulation, which is accelerated by impaired anticoagulant mechanisms, including antithrombin, protein C, thrombomodulin, and tissue factor pathway inhibitor. Damage-associated molecular patterns (DAMPs) accelerate not only tissue factor-dependent coagulation but also the factor XII- and factor XI-dependent activation of coagulation. Inflammatory cytokines are also involved in these changes *via* the expression of tissue factor on endothelial cells and monocytes, the inhibition of anticoagulant systems, and the release of neutrophil elastase from neutrophils activated by inflammatory cytokines. Hyperfibrinolysis in the early phase of PCAS is followed by inadequate endogenous fibrinolysis and fibrinolytic shutdown by plasminogen activator inhibitor-1. Moreover, cell-free DNA, which is also a DAMP, plays a pivotal role in the inhibition of fibrinolysis(11).

The prospective study conducted by Bernd W. Böttiger et.el included 23 patients (29 to 86 years) who underwent out-of-hospital CPR for nontraumatic causes. Blood samples were drawn immediately and 15 and 30 minutes after initiation of CPR. In the case of restoration of spontaneous circulation (ROSC; n=7), additional blood samples were taken immediately, 30 minutes, and 2, 8, 24, 48, and 72 hours after ROSC. A marked activation of blood coagulation was found in all patients. The specific markers of activated blood coagulation and fibrin formation, thrombin-antithrombin complex (TAT; median during CPR, 260 µg/L; median after ROSC, 57 µg/L; normal range, 1.0 to 4.1 µg/L), and fibrin monomers (FM; median during CPR, 34.3 µg/mL; median after ROSC, 65.4 µg/mL; normal range, 0 to 3.6 µg/mL) were markedly increased during and in the early phase after CPR. When patients survived for 48 hours, TAT and FM values returned to the normal range. In most patients, the plasma levels of D-dimer, an indicator of endogenous fibrinolytic activity, were not markedly increased during CPR (median, <0.25 µg/mL; normal range, <0.25 µg/mL) but increased moderately after ROSC (median, 0.56 µg/mL). Levels of plasminogen activator inhibitor type 1 (normal range, 0.3 to 3.5 U/mL), a marker for endogenous inhibition of fibrinolytic activity, were moderately increased in most patients (median during CPR, 4.22 U/mL; median after ROSC, 8.08 U/mL).

The data of the study clearly demonstrate that there is a marked activation of blood coagulation and fibrin formation after prolonged cardiac arrest and CPR in humans that is not balanced adequately by concomitant activation of endogenous fibrinolysis. These changes may contribute to reperfusion disorders, such as the cerebral "no-reflow" phenomenon, by inducing fibrin deposition and formation of microthrombi(12).

In another study conducted by Christophe Adrie, MD et.el. Showed a systemic inflammatory response in out-of-hospital cardiac arrest (OHCA) patients, with increased interleukin-6 and coagulation activity

(thrombin-antithrombin complex), reduced anticoagulation (antithrombin, protein C, and protein S), activated fibrinolysis (plasmin-antiplasmin complex), and, in some cases, inhibited fibrinolysis (increased plasminogen activator inhibitor-1 with a peak on day 1). These abnormalities were more severe in patients who died within two days (50 of 67, 75%) and were most severe in patients dying from early refractory shock. The study concluded that Successfully resuscitated cardiac arrest is followed by a systemic inflammatory response and by activation of coagulation, both of which may contribute to organ failure and neurological dysfunction leading to death in patient after successful resucitation(13).

The aim of this study is to sensitize the health care system about the change in the coagulation profile in post CPR and its effect in outcome of CPR in terms of survival of the patients. We aspire to conduct study focusing on the use of these coagulation markers as a parameter for monitoring the post CPR patients and as a result instill appropriate management as early as possible to overcome the Post cardiac arrest syndrome. We aim at using these markers for early diagnosis of PACS and defeat it before it does.

References

[1]. Kwangha Lee, M.D et.el. Department of Internal Medicine, Pusan National University School of Medicine, Busan, Korea. 2012 May 10.4046/trd.2012.72.5.401.

[2]. Nolan, JP, Neumar, RW, Adrie, C, Aibiki, M, Berg, RA, Böttiger, BW, Callaway, C, Clark, RS, Geocadin, RG, Jauch, EC, Kern, KB, Laurent, I, Longstreth, WT, Merchant, RM, Morley, P, Morrison, LJ, Nadkarni, V, Peberdy, MA, Rivers, EP, Rodriguez-Nunez, A, Sellke, FW, Spaulding, C, Sunde, K, Hoek, TV Post-cardiac arrest syndrome: Epidemiology, pathophysiology, treatment, and prognostication. A Scientific Statement from the International Liaison Committee on Resuscitation; the American Heart Association Emergency Cardiovascular Care Committee; the Council on Cardiovascular Surgery and Anesthesia; the Council on Cardiopulmonary, Perioperative, and Critical Care; the Council on Clinical Cardiology; the Council on Stroke.. *Resuscitation*. (2008). *79* 350–79 [Article] [PubMed].

[3]. Neumar RW, Nolan JP, Adrie C, Aibiki M, Berg RA, Böttiger BW, et al. Post-cardiac arrest syndrome: epidemiology, pathophysiology, treatment, and prognostication. A consensus statement from the International Liaison Committee on Resuscitation (American Heart Association, Australian and New Zealand Council on Resuscitation, European Resuscitation Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Council of Asia, and the Resuscitation Council of Southern Africa); the American Heart Association Emergency Cardiovascular Care Committee; the Council on Cardiovascular Surgery and Anesthesia; the Council on Cardiopulmonary, Perioperative, and Critical Care; the Council on Clinical Cardiology; andtheStrokeCouncil. Circulation (2008) 118:245283.10.1161/CIRCULATIONAHA.108.190652 [PubMed] [CrossRef] [Google Scholar.]

[4]. Adrie C, Adib-Conquy M, Laurent I, Monchi M, Vinsonneau C, Fitting C, et al.Successful cardiopulmonary resuscitation after cardiac arrest as a "sepsis-like" syndrome. Circulation (2002) 106:562–8.10.1161/01.CIR.0000023891.80661.AD [PubMed] [CrossRef] [Google Scholar].

[5]. 11. Adrie C, Monchi M, Laurent I, Um S, Yan SB, Thuong M, et al. Coagulopathy after successful cardiopulmonary resuscitation following cardiac arrest: implication of the protein C anticoagulant pathway. J Am Coll Cardiol (2005) 46:21–8.10.1016/j.jacc.2005.03.046 [PubMed] [CrossRef] [Google Scholar].

[6]. 15. Wada T, Gando S, Mizugaki A, Yanagida Y, Jesmin S, Yokota H, et al.Coagulofibrinolytic changes in patients with disseminated intravascular coagulation associated with post-cardiac arrest syndrome – fibrinolytic shutdown and insufficient activation of fibrinolysis lead to organ dysfunction. Thromb Res (2013) 132:e64–9.10.1016/j.thromres.2013.05.010 [PubMed] [CrossRef] [Google Scholar].

[7]. 16. Gando S, Kameue T, Nanzaki S, Nakanishi Y. Massive fibrin formation with consecutive impairment of fibrinolysis in patients with out-of-hospital cardiac arrest. Thromb Haemost (1997) 77:278–82. [PubMed] [Google Scholar].

[8]. 17. Gando S, Nanzaki S, Morimoto Y, Kobayashi S, Kemmotsu O. Tissue factor and tissue factor pathway inhibitor levels during and after cardiopulmonary resuscitation. Thromb Res (1999) 96:107–13.10.1016/S0049-3848(99)00073-0 [PubMed] [CrossRef] [Google Scholar].

[9]. 12. Böttiger BW, Motsch J, Bohrer H, Boker T, Aulmann M, Nawroth PP, et al.Activation of blood coagulation after cardiac arrest is not balanced adequately by activationofendogenousfibrinolysis. Circulation (1995) 92:25728.10.1161/01.CIR.92.9.2572 [PubMed] [CrossRef] [Google Scholar].

[10]. 19. Gotoh O, Asano T, Koide T, Takakura K. Ischemic brain edema following occlusion of the middle cerebral artery in the rat. I: The time courses of the brain water, sodium and potassium contents and blood-brain barrier permeability to 125I-albumin. Stroke (1985) 16:101–9.10.1161/01.STR.16.1.101 [PubMed] [CrossRef] [Google Scholar].

[11]. Takeshi Wada, Division of Acute and Critical Care Medicine, Department of Anesthesiology and Critical Care Medicine, Hokkaido University Graduate School of Medicine, Sapporo, Japan, 10.3389/fmed.2017.00156.

[12]. Bernd W. Böttiger, Johann Motsch, Hubert Böhrer, Thomas Böker, Michael Aulmann, Peter P. Nawroth and Eike Martin. 1 Nov 1995 .1995;92:2572–2578.

[13]. Christophe Adrie, MD,* Mehran Monchi, MD,† Ivan Laurent, MD,† Suzan Um, BS,‡ S. Betty Yan, PHD,‡ Marie Thuong, MD,* Alain Cariou, MD,§ Julien Charpentier, MD,§ Jean François Dhainaut, MD§. Vol. 46, No. 1, 2005 © 2005 by the American College of Cardiology Foundation ISSN 0735-1097/05/$30.00 Published by Elsevier Inc. doi:10.1016/j.jacc.2005.03.046.

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