# CPFA (Coupled Plasma Filtration Adsorption) prevents renal damage by inhibition of tubular apoptosis and endothelial dysfunction in a swine model of sepsis-induced acute kidney injury (AKI)

G Castellano[1], A Stasi[1], AM Di Palma[1], M Gigante[1], GS Netti[2], C Curci[3], A Intini[1], C Divella[1], C Prattichizzo[2], E Fiaccadori[4], G Pertosa[1], G Grandaliano[2] and L Gesualdo[1]

[1]Department of Emergency and Organ Transplantation, Univ. of Bari, Bari, Italy; [2]Department of Medical and Surgical Sciences, Univ. of Foggia, Italy; [3] Consorzio Carso, Valenzano (Ba), Italy; [4]Department of Clinical and Experimental Medicine, Univ. of Parma, Italy

**Background:** Sepsis has been well recognized as a systemic inflammatory response (SIRS) to an active infectious process in the host and it is a common cause of AKI. Activation of endothelial cells (EC) and tubular apoptosis play a key role in AKI.

The use of sorbents, typically resins, in extracorporeal therapy in particular CPFA, has revealed an improvement in the procedures of blood detoxification.

**Aim:** to investigate to test the efficacy of CPFA in preventing endothelial dysfunction and renal damage in a swine model of sepsis-induced AKI

**Methods:** after 3 h from LPS infusion, 8 pigs were treated with CPFA for 6 h; 8 control pigs receive no treatment. Renal biopsies were performed before (T0) and 9 hours (T9) after LPS infusion.

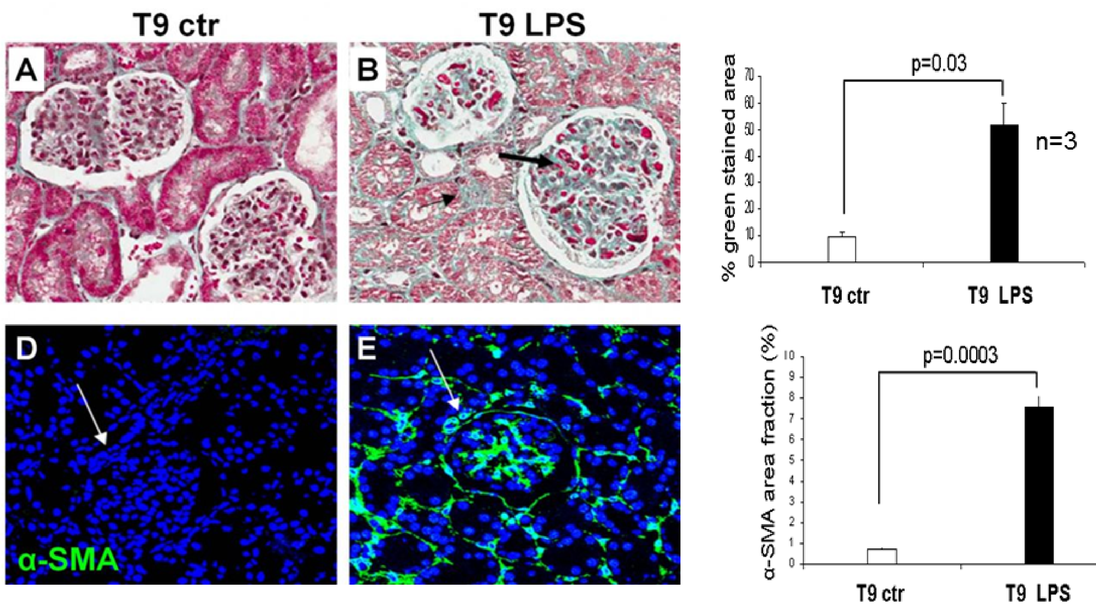


**Fig1: Collagen deposits and α-SMA expression in Swine model of sepsis induced AKI.** Masson's trichrome staining revealed an early fibrosis at the interstitial level and diffuse glomerular thrombi at T9 in septic pig (B-C) respect to control (A) An interstitial increase of the myofibroblast marker α -SMA was observed in septic pigs (F) compared to T9 ctr (E).

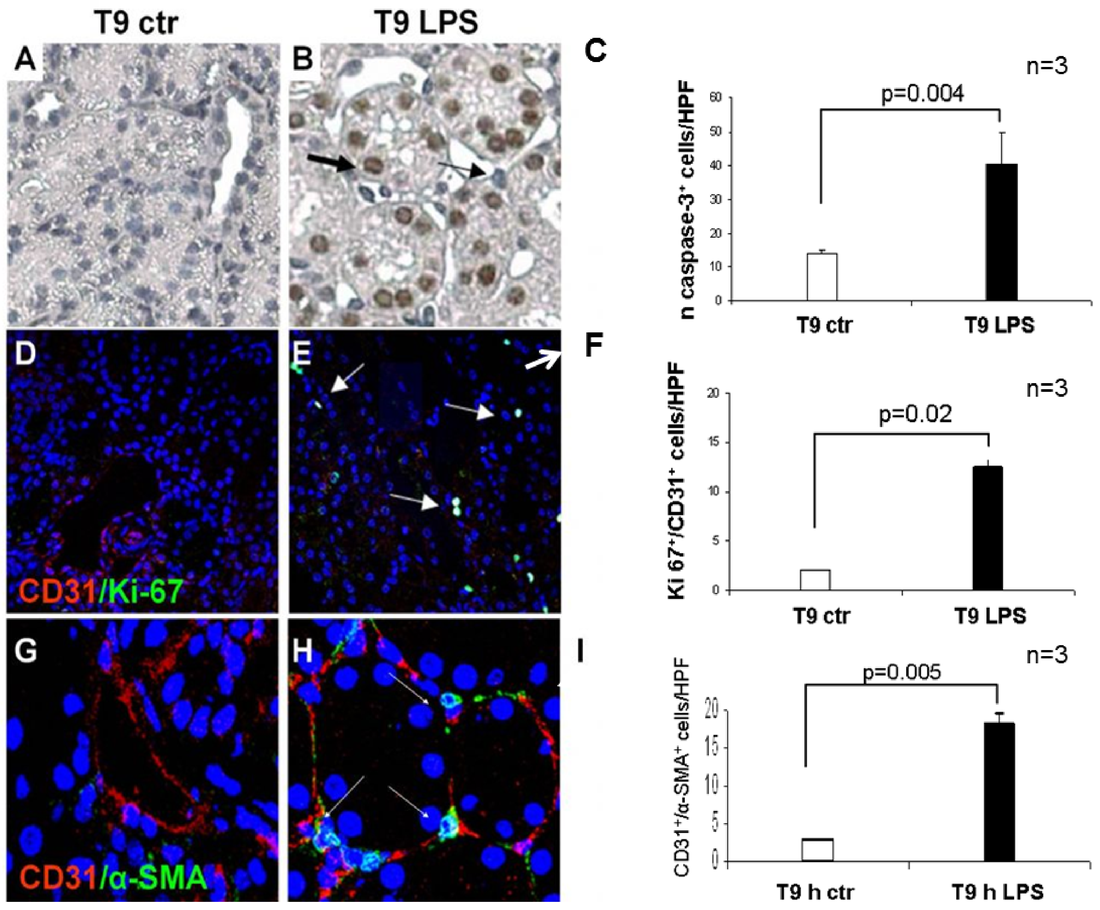


**Fig2: Tubular apoptosis and Endothelial Dysfunction.** Immunohistochemical analysis for Caspase-3 showed intense apoptosis of tubular cells (B-C) but rare apoptotic EC (B). On the contrary, we found **CD31+/Ki-67+** proliferating EC (E-F), expressing **α-SMA** (H-I), a marker of endothelial de-differentiation.

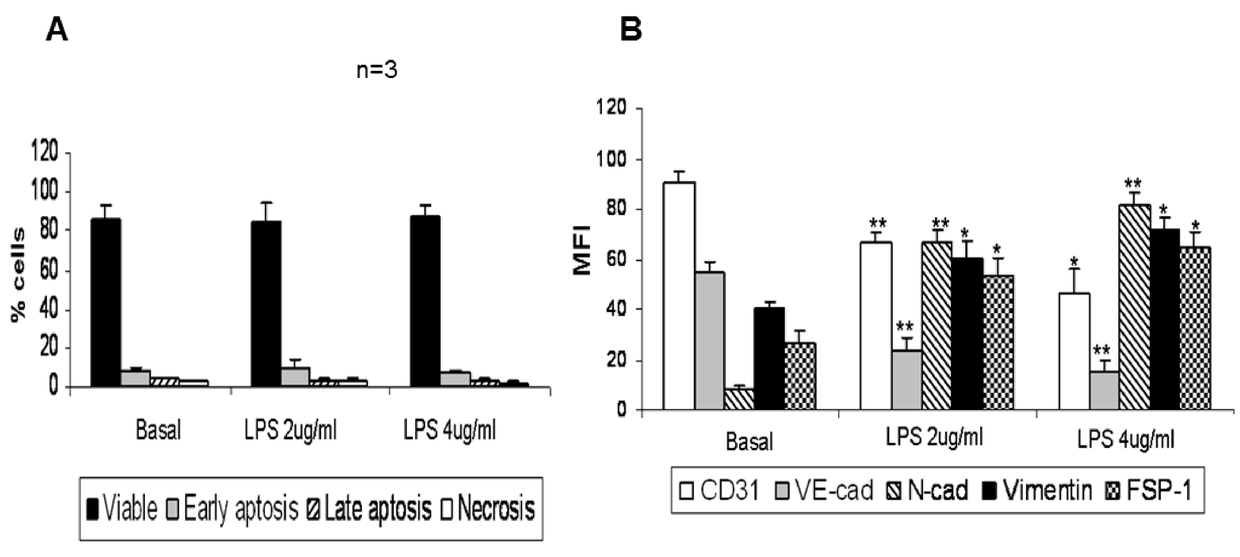


**Fig3: Effects of LPS on ECs in vitro.** Flow cytometry analysis showed that LPS did not affect EC viability (AnnV / IP) (A) and induced phenotypic changes of EC characterized by decreased expression of specific endothelial markers such as CD31 and VE-cadherin and and up-regulation of de-differentiation marker as N-cadherin, Vimentin and FSP-1 (B).

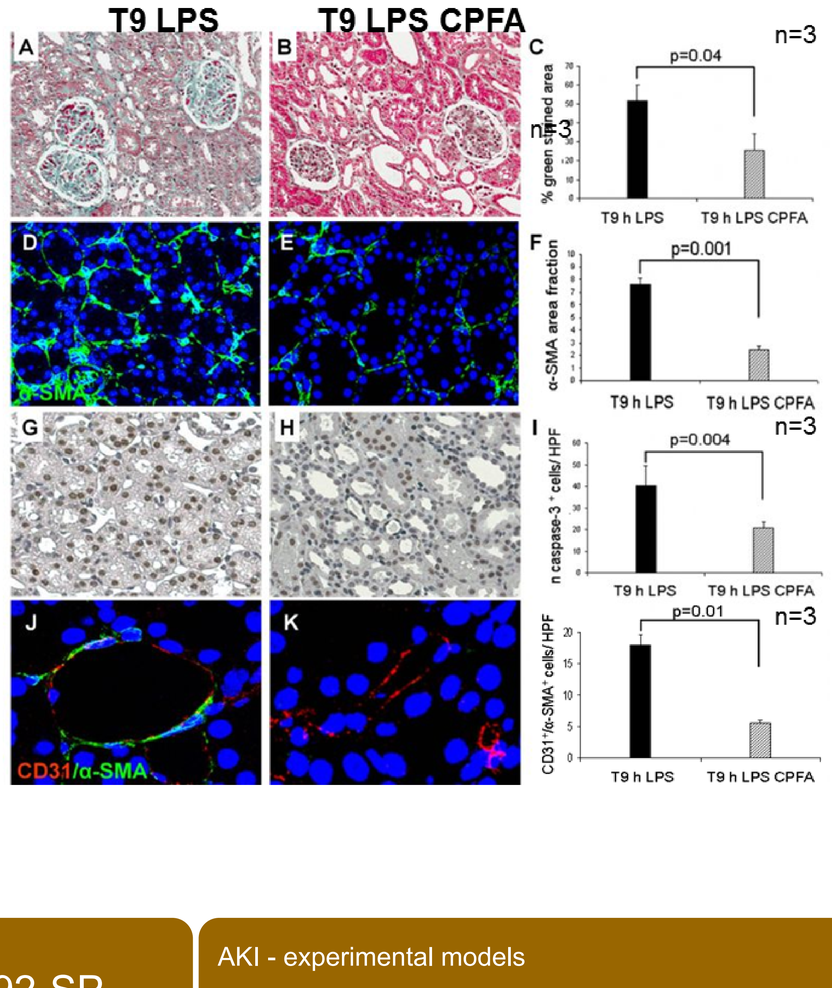


**Fig4: Effects of CPFA treatment.** CPFA treated pigs showed a significant reduction in collagen deposits and glomerular thrombi (B-C) compared to untreated animals(A). Overall, alpha-SMA expression (E-F), as well as endothelial dysfunction (H-I) were strongly reduced by CPFA treatment.

**Conclusion:** Our data demonstrated the occurrence of endothelial dysfunction, tubular apoptosis and renal fibrosis in sepsis-induced AKI. CPFA treatment might be pivotal to counteract the detrimental effects of LPS on renal tissue.

**References:**

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DOI: 10.3252/pso.eu.50era.2013