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Franciosa J A, Guiha N H, Limas C J, Rodriguera E & Cohn J N. Improved left ventricular function during nitroprusside infusion in acute myocardial infarction. *Lancet* 1:650-4, 1972.

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The potent vasodilator sodium nitroprusside was infused into 15 patients with acute myocardial infarction complicated by left ventricular failure, resulting in marked improvement in left ventricular performance characterized by a rise in cardiac output and fall in left ventricular filling pressure without tachycardia or significant hypotension. Thus, vasodilators, by reducing afterload, might offer a rational new approach to the management of heart failure. [The *SCI*® indicates that this paper has been cited in over 470 publications since 1972.]

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This study was performed at the Veterans Administration Hospital and Georgetown University, Washington, DC. At the time this project was conceived, the coauthors, under the direction of Jay N. Cohn, were performing some of the first bedside hemodynamic measurements in patients with shock, severe heart failure, and other low cardiac output states. We had observed in patients with acute left ventricular failure due to uncontrolled hypertension that rapid lowering of the blood pressure, with no other intervention, resulted in prompt hemodynamic and symptomatic improvement. Given the very poor results of treatment of heart failure complicating acute myocardial infarction, we wondered if rapid blood pressure reduction might not be beneficial in this setting. Since these patients often had high filling pressures and systemic vascular resistance, both of which are undesirable in the setting of acute myocardial ischemia, there seemed to be a good pathophysiological rationale for this therapeutic approach. However, prevailing thinking at the time held that lowering of blood pressure in acute myocardial infarction was dangerous and to be avoided. In fact, the use of nitroglycerin was felt to be contraindicated in the face of established acute myocardial infarction. Nevertheless, we proceeded with the study after obtaining all appropriate institutional and individual consents.

A major problem was the lack of an available ideal agent whose only effect should be direct peripheral vasodilation without anti-adrenergic or direct cardiac activity. Sodium nitroprusside had been used many years earlier and appeared to meet these requirements, but was not commercially available. With great trepidation, but under the reassuring guidance of Cohn, our research nurses reluctantly mastered the process of preparing and packaging sterile solutions of sodium nitroprusside, which has since become commercially available as a direct result of its success in these studies. When our first patient who received nitroprusside experienced prompt and dramatic improvement in hemodynamics and symptoms without side effects, our nurses breathed a great sigh of relief. All of us at the patient's bedside expressed mixed feelings of pleasant surprise, anxiety, and awe and understood that much work lay ahead. Our results were quickly confirmed by others.[1]

This study gave rise to numerous large clinical trials of vasodilators in acute myocardial infarction.[2,3] It became an important, frequently cited study because it was innovative and introduced the new concept into clinical practice that performance of the failing heart could be favorably manipulated by intervening peripherally to the heart. It had been accepted that direct cardiac stimulation was the principal means of improving cardiac function. This study played a major role in stimulating the extensive research into the pathophysiology and treatment of heart failure during the past decade.[4,5] All of the coauthors involved in this study have spent all or part of their subsequent careers in academic medicine pursuing research that derived largely from this study. It was particularly gratifying to see this work culminate in approval of the first vasodilator for use in treating heart failure and to play a role in the introduction and development of a new clinical therapeutic modality.[6] This is especially rewarding when we recall that the original manuscript of this study was rejected by another journal because it was thought to be too radical a departure from conventional treatment at the time, although the reviewers had no major scientific criticism of the work.

1. **Chatterjee K, Parmley W W, Ganz W, Forrester J, Walinsky P, Crexells C & Swan H J C.** Hemodynamic and metabolic responses to vasodilator therapy in acute myocardial infarction. *Circulation* 48:1183-93, 1973. (Cited 455 times.)
2. **Cohn J N, Franciosa J A, Francis G S, Archibald D, Tristani F, Fletcher R, Montero A, Cintron G, Clarke J, Hager D, Saunders R, Cobb F, Smith R, Loeb H & Settle H.** Effect of short-term infusion of sodium nitroprusside on mortality rate in acute myocardial infarction complicated by left ventricular failure: results of a Veterans Administration Cooperative Study. *N. Engl. J. Med.* 306:1129-35, 1982.
3. **Flaherty J T, Becker L C, Bulkley B H, Weiss J L, Gerstenblith G, Kallman C H, Silverman K J, Wei J Y, Pitt B & Weisfeldt M L.** A randomized prospective trial of intravenous nitroglycerin in patients with acute myocardial infarction. *Circulation* 68:576-88, 1983.
4. **Guiha N H, Cohn J N, Mikulic E, Franciosa J A & Limas C J.** Treatment of refractory heart failure with infusion of nitroprusside. *N. Engl. J. Med.* 291:587-92, 1974. (Cited 250 times.)
5. **Cohn J N & Franciosa J A.** Vasodilator therapy of cardiac failure. (Parts 1 and 2.) *N. Engl. J. Med.* 297:27-31; 254-8, 1977. (Cited 335 times.)
6. **Captopril Multicenter Research Group.** A placebo-controlled trial of captopril in refractory chronic congestive heart failure. *J. Amer. Coll. Cardiol.* 2:755-63, 1983.

