Role of Positive Inotropic Drugs in the Intensive Care Unit

Essay Submitted for Partial Fulfillment
of Master Degree in General Intensive Care Medicine

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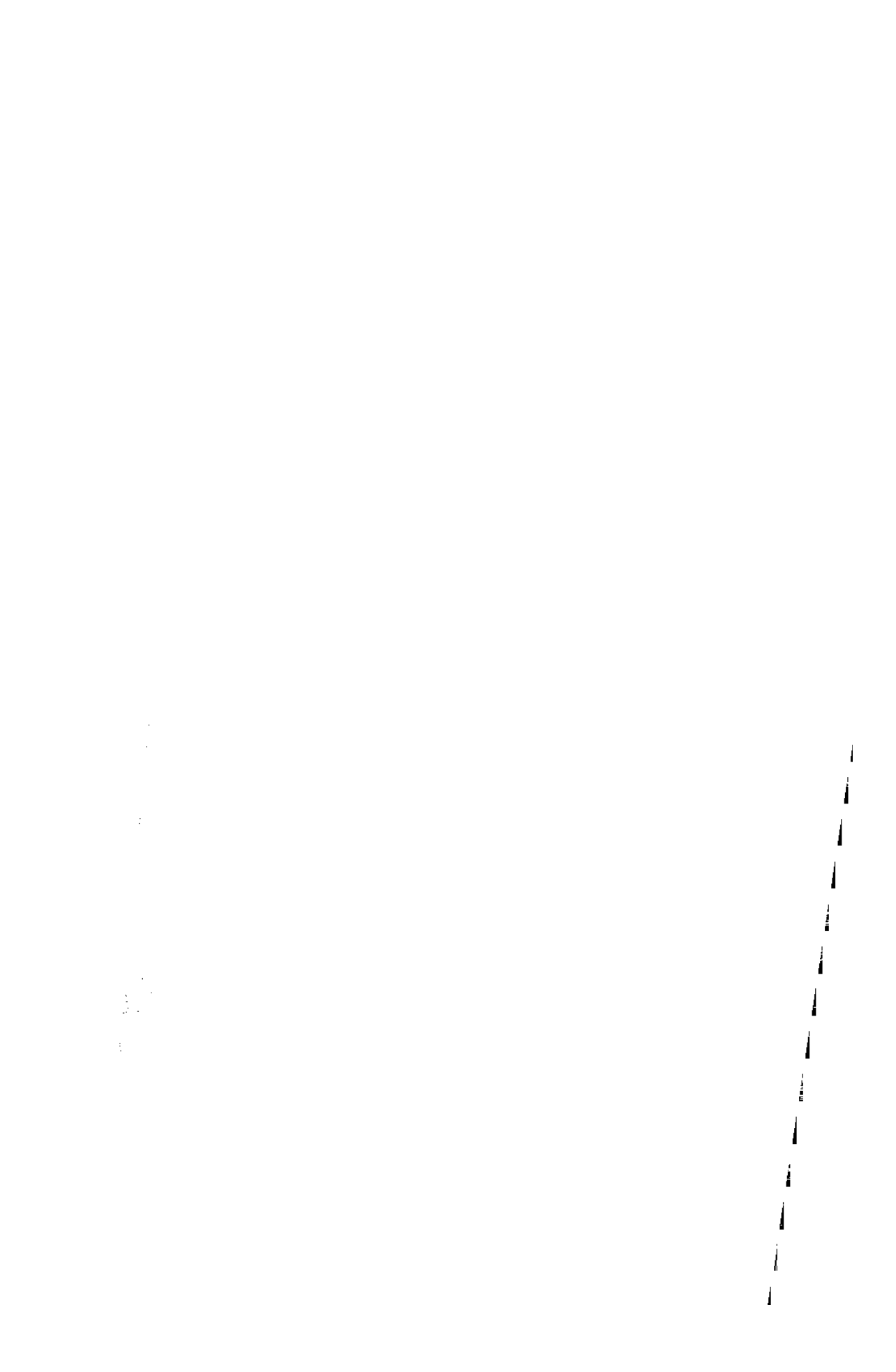

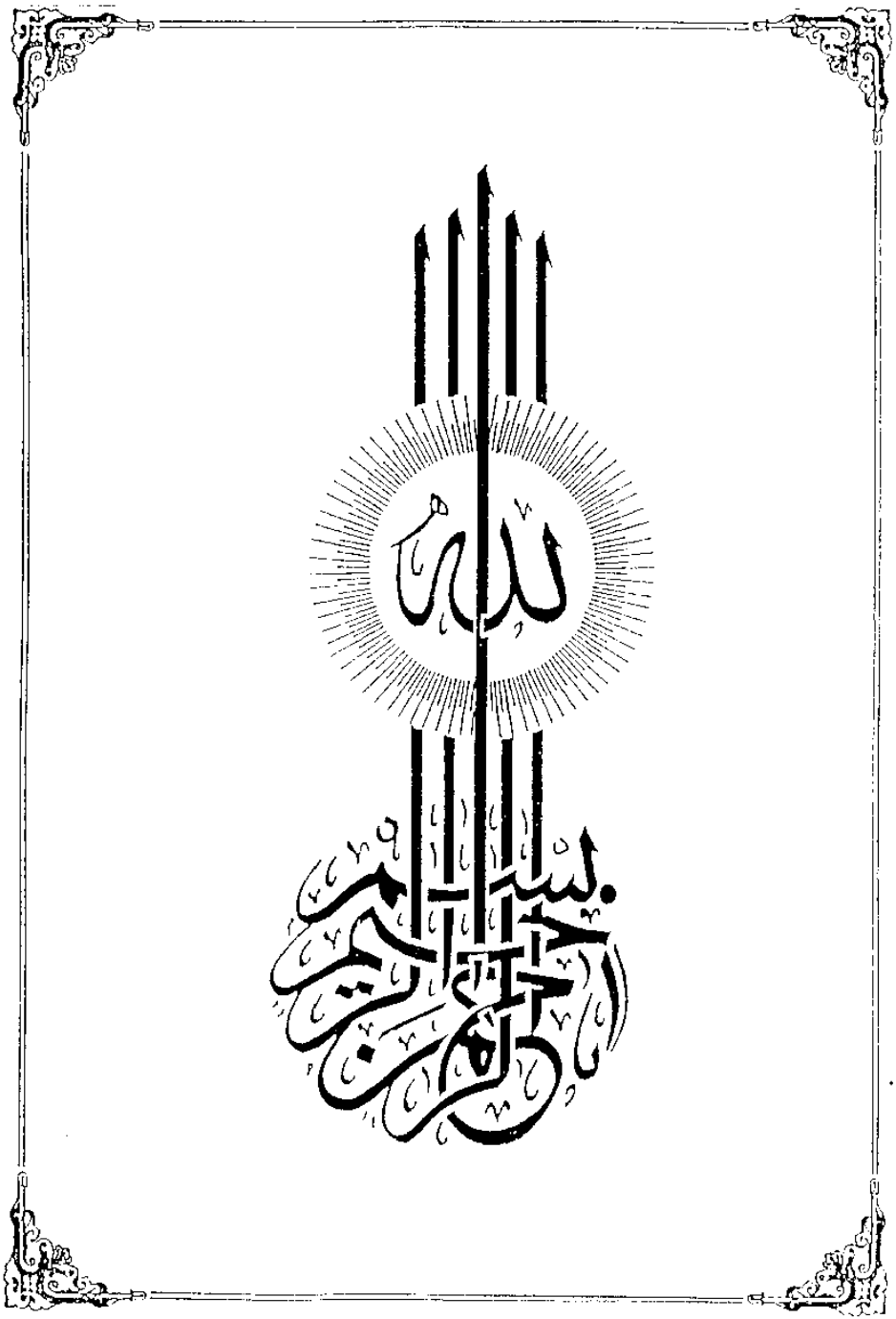

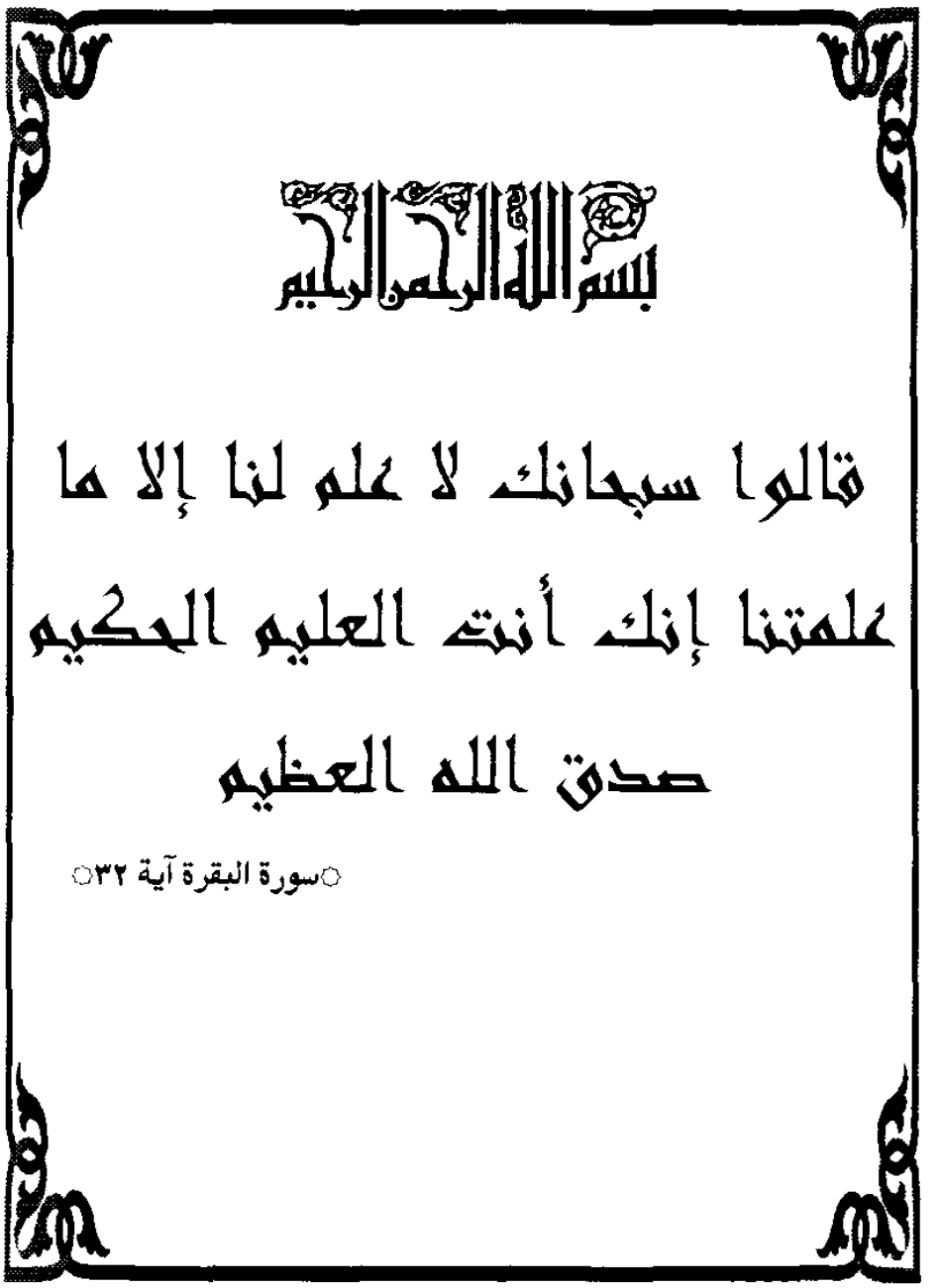

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Alaa El Din Koraa

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Introduction

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Positive inotropic agents are considered amongst the most widely used drugs in intensive care units. It is not only a method to increase myocardial contractility in heart failure but improvement in splanchnic circulation is possibly even more important, given the postulated role of the gut and liver in the pathogenesis of sepsis syndrome and multiorgan failure (MOF). ***(Ruokonen, et al.,1993)***

Achievement of the highest readily attainable cardiac index (CI) and oxygen delivery (DO_2) while maintaining an adequate arterial pressure could be a reasonable goals to use positive inotropics in critically ill patients.

"Congestive Heart Failure" is a traditional term for the complex system of signs and symptoms caused by chronic myocardial cell loss, secondary neurohormonal and vascular changes, and their consequences. This label is imprecise, because abnormalities other than myocardial dysfunction can result in similar findings, while different myocardial insults, at various stages of progression, can display broad spectra of clinical findings. Precise physiological diagnosis is important in the critical care sitting, where multi-system disease, multiple drug therapy, and rapid clinical changes can mask, mimic or produce myocardial dysfunction. ***(Stephen, 1994)***

Systolic failure is present when systemic blood flow is insufficient to meet the needs of peripheral tissues; neither arterial hypotension nor a low cardiac index perse is a prerequisite for diagnosis. Diastolic failure is present when ventricular filling pressure (and, therefore pulmonary or systemic central venous pressure) exceeds tolerable levels, causing pathologic consequences (pulmonary edema, hepatic, or systemic congestion); similarly, this definition does not include a specific end-diastolic pressure, for many factors can influence a patient's tolerance of a given venous pressure. Both definitions should restrict the diagnosis of heart failure to abnormalities of myocardial performance. ***(Morgan, et al., 1991)***

The low cardiac output syndrome which follows open heart surgery deserves special considerations. In this situation, the loss of myocardial contractility leading to acute heart failure is mainly the result of ischemic stress on the myocardium, which can be provoked by the operation or cardioplegia, and excessive work load due to pressure or volume overload. This is reversible in principle, provided the sources of myocardial energy are able to recover after extracorporeal circulation. ***(Hensley and Martin, 1995)***

In acute congestive heart failure due to myocardial ischemia, intracellular acidosis and the accumulation of phosphate may be the initial underlying causes of contractile failure, while minutes later lack of energy compounds may be an important constituting factor. ***(Hensley and Martin, 1995)***

The cause of contractile failure in chronic syndromes is less well understood. There is evidence for the desensitization of β-receptors on the cell surface but the precise location of the defect is unclear. The receptors may be down - regulated in addition to abnormalities in several other parts of the contractile pathway including the contractile protein and the sarcoplasmic reticulum. Deficiency of cyclic adenosine monophosphate (cAMP) has also been suggested as a mechanism of contractile failure. ***(Morgan and Mikhail, 1996)***

In both acute and chronic congestive heart failure, there is redistribution of blood flow to the body organs. Of particular significance is the reduction of blood flow to the kidneys, and a reversal of this defect is one of the major therapeutic objectives. ***(Cohen, 1990)***

Positive inotropic drugs, vasodilators and drugs altering relaxation of the myocardium have been evaluated in the treatment of heart failure. Pure inotropic drugs can cause tachycardia, ischemia and "metabolic exhaustion" of the myocardium. The most advantageous profile for an (inotropic) drug in many patients with low cardiac output syndrome would be a drug combining systemic vasodilatation, renal vasodilatation, increased relaxation of the myocardium, only a mild positive inotropic effect, and no chronotropic effect. ***(Katz, 1986)***

Before attempting to determine the physiological aberrations producing heart failure in a patient, extramyocardial causes of low flow and congestive states must be excluded. In a critically ill patient cardiovascular disorders can mimic systolic dysfunction, reducing cardiac output by inhibiting antegrade flow (valvular stenosis, thrombosis, embolus, pericardial disease, or arterial hypertension) or permitting retrograde ejection (valvular insufficiency or septal defects). Obstructing and regurgitant lesions can also imitate diastolic dysfunction, as can other disorders, such as intravascular hypervolemia and pulmonary injury (ARDS). Extra myocardial lesions may in fact produce their effects by altering cardiac performance or cause heart failure as a secondary phenomenon. ***(Katz, 1990)***

The immediate therapeutic goals should seek to improve the acute hemodynamic abnormalities. Compromised organ perfusion may require augmentation of ventricular contractility, reduction in afterload components, volume loading or venoconstriction to increase preload, or a combination of these interventions. Treatment of other acute precipitating or complicating events (severe anemia, electrolyte abnormalities, fever, hypoxia) is included with the immediate goals of therapy. ***(Stephen, 1994)***

The term " **shock** " is commonly used but ill defined. The conditions to which it is applied vary in etiology, pathology and presentation so that the value of the term even as a clinical description is frequently challenged, however, the most widely accepted definition is a state of generalized impairment of the function of vital organs due to acute circulatory inadequacy including abnormalities of pressure, flow or distribution of blood supply. There are also circumstances in which excessive metabolic demands may render the circulation inadequate. ***(Roe and Kinney, 1965)***

The reduction of the sympathetic outflow, spinal anesthesia and some drugs may cause hypotension that is predominantly postural. Since vascular smooth muscle is still responsive to the mediators in this situation, any sympathomimetic can be used to restore the blood pressure. It should be emphasized that hypotension is not necessarily the same as shock. ***(Spoerel et al.,1964)***

If cardiac output and tissue perfusion are well maintained, hypotension does not require vigorous treatment. Acute or chronic insufficiency is generally characterized by alternation of cardiac output and relative failure to deliver sufficient blood flow to meet the metabolic demands of vital organs. ***(Spores and Dewood, 1979)***

The term pump failure refers to that group of patients with shock in whom the circulatory insufficiency is directly related to impaired pumping ability of the left ventricle ***(Hurst, 1982)***

Heart failure is common in all forms of shock, accordingly over the past several years the mainstay of drug therapy of circulatory insufficiency has been various inotropic agents. Cardiac dysfunction occurring in the perioperative period in patients that may be admitted to an I. C. U., requires prompt diagnosis and intervention. Selection of the appropriate treatment depends on an understanding of the pathophysiological mechanisms involved, identification of the cause of inadequate peripheral perfusion, and correction of extra cardiac factors that may be contributing to low cardiac output. ***(Lappas et al., 1977)***

At least four potential problems must be considered when a patient with heart failure is given a positive inotropic drug ***(Katz, 1983).*** The first arises from the fact that any drug that increases the work of hypertrophied heart can be expected also to increase the rate of energy expenditure; if this over - taxes the ability of the failing heart to supply high energy phosphate to the contractile proteins, the inotropic drug may accelerate myocardial cell death and so can hasten the demise of the patient ***(Lesch, 1976).*** Although of clear relevance in patients with ischemic heart disease, this consideration may also apply to the chronically overloaded myocardium in patients with such conditions as cardiomyopathy and vascular disease.***(Meerson, 1969)***

Second, patients with heart failure often suffer from abnormalities of relaxation as well as contraction, so that when pump function is compromised more by an abnormality of relaxation (Lusitropic) than of contractility (inotropic), use of purely inotropic drug may increase clinical disability. ***(Smith and Katz, 1983)***