Acute renal failure (ARF) occurs when the kidneys fail to eliminate nitrogenous waste products and to maintain homeostasis of water and electrolytes [1]. The consequences of this derangement can (if not reversed on time) precipitate a syndrome that can interfere with the already difficult management of intensive care unit (ICU) septic patients and worsen their prognosis.

Historically, many different definitions have been provided for ARF in different studies, which makes it difficult to compare experiences and explains the wide range of figures reported on incidence or mortality. The concept is still evolving, but recently some consensus has been reached that allows us to define our understanding of ARF, or even better of acute kidney injury (AKI). The term “acute kidney injury” is a step forward that stresses the necessity to detect and provide support for this problem in the early stages of the process, before there is complete failure of the kidneys.

As stated, the main problem in addressing the epidemiology of AKI is the lack of consensus on the definition of this process [2]. It is universally accepted that uncomplicated AKI as a whole is a process with a low incidence and a good prognosis. Although this statement is generally true (the mortality rate is under 5%) [3], we must accept that AKI is not an accompanying phenomenon and that per se it affects survival independently and significantly. In a recent study by Levy et al. on patients undergoing procedures with radiocontrast agents, the investigators detected that ARF was associated with an odds ratio of 5.5 for mortality [4]. Moreover, when AKI develops in the hospital setting it is associated with poorer outcome [5], and in these cases, hypovolemia, ischemia, or toxic acute tubular necrosis (ATN) is the predominant cause [6].
The prevalence of ARF in ICUs approaches 5% in most studies (5.7% in the multicenter international study BEST or 5.6% in Spanish ICUs), and when septic shock is present, prevalence is over 50% [6–8]. Mortality is over 40% and higher than that predicted by SAPS II, and when complicated by severe sepsis in the ICU mortality rises to 50–70%. These figures have not improved for several decades [5, 9]. On the other hand, more than 85% of patients who survive the episode are dialysis-independent at discharge.

2 AKI and Sepsis

The exact mechanisms and sequence of events resulting in renal dysfunction in sepsis are poorly understood, but we know that over 90% of AKI episodes in the ICU are either prerenal dysfunction or ATN [6] and these two processes share a common origin: hypoperfusion. Sepsis induces cytokine-mediated (tumor necrosis factor, interleukin-1, and chemokines) nitric oxide synthesis leading to a decrease in systemic vascular resistance. This implies a low effective circulating volume, predisposing patients to acute renal failure. This environment could be worsened by loss of fluids (third space, hemorrhage, etc.) and/or low cardiac performance. In addition, this arterial vasodilatation is sometimes resistant to exogenous catecholamine. An increase of hydrogen ions and lactate in plasma concentrations and a decrease of ATP in vascular smooth muscle cells cause hyperpolarization of the vascular smooth muscle cells. Furthermore, the high endogenous levels of vasoactive hormones during sepsis may be associated with downregulation of their receptors, which would result in a weakening of their effects on the vasculature. Furthermore angiotensin II and endothelin, which try to support arterial tone, also cause renal vasoconstriction and predispose patients to acute renal failure [10]. The procoagulant state seen in sepsis can also lead to disseminated intravascular coagulation, which is related to glomerular thrombi and acute renal failure.

Regarding the clinical impact of this relationship, sepsis is the main predisposing factor for AKI development in the ICU [11], and AKI is present in more than 50% of patients with septic shock [12]; this figure could be even higher if we look closely for its presence [13]. As already stated, the combination of AKI and sepsis is associated with up to 70% mortality, as compared with 45% mortality among patients with AKI alone. Finally, it is also recognized that untreated ARF may contribute to a higher incidence of new-onset sepsis [4].

3 Definition and Stratification of AKI

It can be said that there are as many definitions of AKI as studies published. Moreover, until recently all the diagnostic criteria were based on isolated determinations of different markers for renal function with arbitrary levels for defining abnormality.

A sensible definition for AKI could be: “a sudden loss of renal function followed by alterations in electrolyte, acid–base, and fluid homeostasis”. This seems a clear statement but is prone to different interpretations: What do we understand by “sudden”? Which