



## UPDATE IN INTENSIVE CARE MEDICINE: HEMODYNAMIC MONITORIZATION IN THE CRITICAL PATIENT

# Evidence on the utility of hemodynamic monitorization in the critical patient<sup>☆</sup>

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### KEYWORDS

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### PALABRAS CLAVE

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**Abstract** Hemodynamic monitoring is a tool of great value for the assessment of critically ill patients. It can not only detect and determine the source of hemodynamic instability, but also guide the choice of appropriate treatment and further evaluate its effectiveness. However, monitoring *per se* is not a therapeutic tool and its use in the absence of a well-defined objective, need not affect patient outcome. To improve outcome, hemodynamic monitoring necessarily must be coupled to a treatment protocol that has effectively been shown to improve outcome. Accordingly, the usefulness of monitoring systems should be evaluated not only on the basis of the accuracy and reliability of their measurements, but also on the ability to positively affect patient outcome. In this regard, many of the arguments against the use of hemodynamic monitoring are a consequence of non-protocolized use and of application not directed toward specific hemodynamic objectives of proven benefit for the patient.

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### Evidencia de la utilidad de la monitorización hemodinámica en el paciente crítico

**Resumen** La monitorización hemodinámica es una herramienta de indudable valor para la evaluación de los pacientes críticos. Nos permite no solo detectar y determinar el origen de la inestabilidad hemodinámica, sino también guiar la elección del tratamiento más adecuado y evaluar con posterioridad su efectividad. Sin embargo, la monitorización *per se* no constituye una herramienta terapéutica y su empleo, sin un objetivo claramente definido, no tiene por qué afectar a la evolución de los pacientes. Para que la monitorización hemodinámica redunde en beneficio para este debe ir necesariamente acoplada a un protocolo de tratamiento que efectivamente haya demostrado mejorar su pronóstico. En consecuencia, la utilidad de los sistemas de monitorización no debería evaluarse tan solo por la exactitud y fiabilidad de sus medidas, sino también por la capacidad de afectar favorablemente a la evolución de los pacientes. En este sentido, gran parte de los argumentos utilizados en contra del empleo de la monitorización

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hemodinámica tienen su origen en un uso no racionalizado de la misma y en la aplicación no dirigida a objetivos hemodinámicos concretos y de demostrado beneficio para el paciente.

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## Introduction

Clinical management of the critically ill patient often faces complex problems which intensivists traditionally have tried to solve by applying pondered criteria based on the consultation of textbooks, medical journals in the field, or requesting the opinion of experts. However, many of these textbooks, and even some review articles published by reputed journals, are the result of the subjective collection of evidence rather than of a systematic review of such evidence. As a result, personal opinions not based on the best available evidence at the time are often included. The applied criteria therefore are closer to art than to science, and individual experience, skill or mastery prevail over the thorough, explicit and appropriate use of the best evidence available when it comes to making decisions referred to patient care. This latter approach, known as evidence based medicine (EBM), attempts to integrate the best scientific proof available, i.e., that which affords the best evidence, with the individual clinical experience and values of the patient, with a view to establishing the best clinical decision.<sup>1,2</sup>

The concept of best evidence implies stratification or hierarchical structuring, whereby the highest evidence in the structure should have a greater impact in terms of clinical decision making than observations at a lower level. In this context, EBM proposes the inclusion of randomized clinical studies and their systematic reviews (metaanalyses) as representing the highest level of evidence, i.e., ranking uppermost in the hierarchical structure, though without being the only evidence. Accordingly, we should attribute greater confidence to therapeutic decisions based on a systematic review or on a randomized clinical trial than on lower ranking studies such as observational or physiological studies, for although the latter do contribute evidence, it is weaker than in the case of the higher ranking studies.

However, the application of these concepts is hampered on a daily basis by the reality of clinical practice. In this context, the conduction of randomized clinical trials designed to demonstrate the benefits or futility of hemodynamic monitorization in the critical patient is extremely complex. Recently, different experts have pointed out the important limitations which clinical trials and posterior metaanalyses have in the field of Intensive Care Medicine.<sup>3,4</sup> As an example, it is difficult to analyze and compare different studies involving terms as imprecise as acute respiratory distress syndrome or sepsis, and which encompass very heterogeneous populations.<sup>5</sup> Furthermore, we must take into account that hemodynamic monitorization in itself is not a therapeutic tool, and that in order to offer benefit for the patient, such monitoring must be tied to treatment protocols of established efficacy. On the other hand, these treatment protocols have not been evaluated in most clinical trials.<sup>6,7</sup> Thus, monitorization without defined therapeutic objectives does not affect patient outcome and affords no benefit.<sup>8</sup> Because of these and other reasons, few randomized

clinical trials have been carried out in this area of Intensive Care Medicine, and the justification of hemodynamic monitorization is based more on arguments of a physiological nature than on any other type of arguments.<sup>9</sup> Indeed, the principles of physiology and physiopathology, while not affording evidence as solid as that attributed to clinical trials and metaanalyses, are the elements that help us to advance in our understanding of the processes and disease conditions in the critical patient. When adequately processed and analyzed, they moreover can serve to continue the decision making process - though always accepting a certain degree of trial and error.<sup>10</sup> Based on these arguments, we assume that an improved appreciation of the physiopathology of the treated process and of the mechanism by which treatment results in improvement will facilitate selection of the best management options. Although attractive for the clinician and especially for the investigator, the truth is that physiological arguments are not always validated by clinical studies. Nevertheless, we must be aware that in clinical practice the decision making process cannot be stopped simply because there are no systematic reviews or randomized clinical studies supporting our decisions - though we must be prudent and recognize the type or level of evidence upon which such decisions are supported.

## Monitorization of the critical patient: Septic shock and acute lung injury

The usefulness of a hemodynamic monitorization system should be evaluated considering not only the capacity of the device to correctly measure what it has been designed to measure (cardiac output, for example), since most such systems offer satisfactory performance in this sense.<sup>11</sup> From a practical point of view, hemodynamic monitorization should be evaluated according to its capacity to favorably influence resolution of the disease process and the patient outcome, on the basis of the information provided. In this context, hemodynamic monitorization must be able to detect the presence of hemodynamic instability with hypoperfusion or global tissue hypoxia and, when these conditions already exist, it should help to quickly start the necessary treatment, with due control of its results. Accordingly, the two premises on which the utilization of hemodynamic monitorization is based are:

- (1) Its superiority in diagnosing the presence of hemodynamic instability with global tissue hypoxia versus physical examination
- (2) The benefits obtained with the application of treatment based on predefined hemodynamic objectives.

In effect, routine exploration does not always seem useful for diagnosing tissue hypoxia. In a group of 36 critical patients, the criterion of hemodynamic stabilization based

on normalization of the vital signs was insufficient to guarantee adequate tissue perfusion as reflected by an increase in lactic acid and a drop in central venous oxygen saturation.<sup>12</sup> In a later study, this time involving patients with severe sepsis or septic shock, these same investigators confirmed the incapacity of hemodynamic evaluation based on the physical examination, vital signs, central venous pressure (CVP) and diuresis to detect the persistence of global tissue hypoxia versus the incorporation of continuous central venous oxygen saturation monitorization as a surrogate of cardiac output or oxygen transport.<sup>12</sup>

In patients with acute lung injury (ALI), the capacity of physical examination (capillary filling time > 2 s, spots on the skin of the knees, or cold extremities) to detect tissue hypoperfusion (defined by cardiac index (CI) < 2.5 l/min/m<sup>2</sup> or mixed venous oxygen saturation < 60%) has recently been investigated in the subgroup of 478 patients of the Fluid and Catheter Treatment Trial (FACTT) monitored with the pulmonary artery catheter (PAC).<sup>13</sup> The results of this study revealed low sensitivity of the three clinical signs (12% and 8% in detecting CI < 2.5 l/min/m<sup>2</sup> and SvO<sub>2</sub> < 60%, respectively), with a likewise low positive predictive value (40% and 56%). The authors concluded that in patients with acute lung injury, physical examination is not useful for detecting a reduced cardiac index and/or low mixed venous oxygen saturation. Moreover, after incorporating central venous pressure and fluid loss to the data of the physical examination, the information continued to lack clinical usefulness.

The second issue raised, referred to the capacity of hemodynamic monitorization to favorably influence the outcome of septic shock, has been the subject of a recent review in the form of a metaanalysis including 9 studies out of 29 potential publications comprising 1001 patients.<sup>14</sup> The authors concluded that the application of a "structured quantitative resuscitation" strategy, i.e., interventions targeted to clearly define hemodynamic objectives, within the first 24 h of sepsis, results in a significant decrease in mortality. However, when this strategy was implemented in later stages, it proved futile or even counterproductive. Another aspect underscored by the authors was the variety of the predefined hemodynamic objectives in each of the studies analyzed (oxygen transport, cardiac index or central venous oxygen saturation, for example). Accordingly, in the words of the authors, it is not clear whether any of the therapeutic objectives are superior to the rest, and consequently this issue should be investigated by future studies. As an example, we now know that dynamic measurements of preload-dependency (passive raising of the legs, variation of pulse pressure or of systolic volume, for example) are clearly superior to static measurements (central venous pressure, pulmonary artery wedge pressure, heart chamber areas or volumes, etc.),<sup>15,16</sup> but we do not know whether the implementation of a protocol in which the administration of fluids is based on dynamic measures will afford greater benefits than the use of static measures in this group of patients.<sup>17</sup>

In patients with acute lung injury, the capacity of hemodynamic monitorization to favorably influence the outcome of the process has not been established. Shah et al.,<sup>18</sup> in a metaanalysis of 5051 patients included in 13 clinical trials during a period of 20 years, concluded that the use of the pulmonary artery catheter (PAC) does not increase

mortality or the duration of hospital stay, but also does not afford benefits of any kind. In the opinion of these investigators, the results observed with the use of the PAC could be attributed to the absence of effective treatments based on the information derived from catheter use, due to the lack of a previously defined protocol associated to the monitorization. Coinciding with these observations, Hadian and Pinsky<sup>19</sup> recently concluded that the "general use of the PAC in the critical patient is not associated to changes in mortality or morbidity (level of evidence 1), while in contrast there is a risk of arrhythmias during placement of the catheter and of infection and thrombotic complications when it is maintained for prolonged periods of time (>48 hours)". The recommendation of these authors is to avoid indiscriminate utilization of the PAC, and when the decision is made to use the catheter, it always should be associated to a therapeutic protocol of established efficacy. Lastly, in a recent update of the Cochrane review database,<sup>20</sup> no differences in mortality were found with or without utilization of the PAC, though the costs were found to be higher in the PAC group. Nevertheless, this update again stressed the need for future studies to define the most effective treatment protocols and to establish the groups of patients that may benefit from the PAC, before deciding to abandon its use.

The results of the FACTT study have recently been published.<sup>21,22</sup> This study couples the hemodynamic monitorization of patients with acute lung injury to a treatment protocol fundamentally centered on the way in which fluids are administered (liberally or restrictively). In addition to confirming the benefits of the restrictive strategy, the study shows that monitorization with the PAC versus the measurement of central venous pressure not only affords no benefits but significantly increases the costs.<sup>23</sup> In turn, the authors here again conclude that routine use of the PAC in the critical patient is not justified.<sup>24</sup> However, the FACTT study does not fully address the issue of PAC-guided therapy in patients with acute lung injury, since both delays in placing the PAC (24 h from the start of lung injury and 43 h from admission to the ICU), and the values of the first hemodynamic measurements obtained (cardiac index  $4.2 \pm 1.4$  l/min/m<sup>2</sup> and central venous oxygen saturation  $71.5 \pm 11.2\%$ ),<sup>18</sup> suggest that the patients had already undergone vigorous resuscitation at the time of inclusion in the study. For this reason, in the opinion of some experts,<sup>19</sup> the issue actually addressed by the FACTT study has not been whether or not PAC is useful in guiding initial resuscitation among patients with acute lung injury, but rather whether the technique is useful for limiting the damage and thus for avoiding an increase in lung edema. At present, different experts and investigators continue to regard PAC as useful, at least in some subgroups of patients with ARDS.<sup>25</sup>

The monitorization of lung edema was proposed more than two decades ago by Eisemberg<sup>26</sup> and Mitchell<sup>27</sup> as an alternative to monitorization with the PAC. These authors included a total of 101 patients, of which 52 had ARDS, and subjected them to treatment based on the measurement of lung edema or pulmonary artery wedge pressure. The results showed that the patients treated according to the degree of lung edema received less intravenous fluids, required briefer mechanical ventilation, had a shorter stay in the ICU, and tended to suffer lesser mortality (35% versus 47%)—the patients deriving most benefit being those with lung edema

and no elevation of pulmonary artery wedge pressure. Posterior observational studies have confirmed the relationship between the severity of lung edema and mortality and, more importantly, the relationship between the resolution of lung edema and the final patient outcome.<sup>28,29</sup> Lastly, some investigators and scientific societies have proposed the measurement of lung edema for diagnosing ARDS<sup>30</sup> or for stratifying its severity.<sup>31</sup> As a result, an ever increasing number of experts consider that hemodynamic monitorization, together with the measurement of lung edema, constitute an alternative to PAC monitorization.<sup>32-34</sup>

In sum, in the critical patient, hemodynamic instability with global tissue hypoxia sometimes coincides with stable vital signs, and therefore may go unnoticed. On the other hand, the early application of a structured resuscitation protocol with predefined hemodynamic objectives has been shown to reduce mortality, at least in patients with severe sepsis or septic shock. All this speaks in favor of the use of hemodynamic monitorization to recognize and treat the situation of tissue hypoxia on an early basis. However, it remains to be established what kind of monitorization should be used, since the superiority of one hemodynamic objective over another (such as for example the optimization of preload on the basis of dynamic measurements or the monitorization of lung edema) has not been defined.

## Monitorization in the high risk surgical patient

Major surgery is associated with significant increase in oxygen demand. Under normal conditions, patients with a preserved cardiopulmonary reserve compensate this increase in demand by elevating their cardiac output and tissue oxygen extraction. However, in patients at high risk due to the existing comorbidities and/or the nature of the surgical procedure, this physiological reserve may not be enough to cope with the increase in metabolic demand during surgical stress – thereby making it more likely for tissue hypoperfusion, organ dysfunction and even death to occur.<sup>35</sup> For this reason, the application of a hemodynamic strategy destined to increase the oxygen supply during the perioperative period (even up to 8 hours after surgery<sup>36</sup>), based on the definition of clearly defined hemodynamic objectives, has been shown to improve the prognosis of high risk surgical patients in terms of a reduction in the number of complications, a shortened hospital stay and lesser costs and mortality.<sup>37</sup> Moreover, the benefits of such a strategy appear to have a positive impact not only over the short term but also during the years after its application.<sup>38</sup>

During over two decades, more than 20 randomized studies and several metaanalyses have shown that hemodynamic monitorization offers benefits for high risk surgical patients when accompanied by a protocol ultimately designed to increase tissue oxygen supply with the purpose of avoiding hypoperfusion.<sup>37,39-44</sup> Despite the fact that these high risk patients may represent only a small percentage of the total patients subjected to surgery, their high mortality rate accounts for most of the surgery-related deaths. In global terms, this means that many patients potentially may benefit from such hemodynamic optimization strategies.<sup>45</sup>

Logically, the evolution of hemodynamic optimization and of its therapeutic objectives is closely linked to

technological advances in hemodynamic monitorization. Although in its beginnings the PAC was the prevalent (if not the only) system,<sup>40</sup> the development of new minimally invasive devices such as esophageal Doppler ultrasound or systems based on the analysis of arterial pressure has facilitated the development of therapeutic algorithms with aims that are more easily applicable. Likewise, the therapeutic use in this field of what has been called “functional hemodynamic monitorization”<sup>46</sup> has also allowed rationalization of fluid administration based on the use of dynamic preload-dependency parameters such as variation in systolic volume.<sup>47</sup> As a result, patients receive the required amounts of fluid at the appropriate time, with a view to avoiding the development of tissue hypoperfusion.

It is interesting to note that despite the large body of evidence gained (in many cases greater than that supporting some of the recommendations commonly accepted today), hemodynamic optimization has not received generalized or uniform acceptance,<sup>48</sup> except possibly for some counted exceptions.<sup>49</sup> The reasons for this low acceptance and heterogeneous implementation appear to be complex and multifactorial,<sup>45,50</sup> but seem to involve factors such as increased resource requirements (and thus possibly also greater cost), the need for more continuous and personalized care on the part of the physician, and the apparent confusion produced by the diversity of the available hemodynamic objectives. However, despite some ambiguities, it seems obvious that hemodynamic optimization strategies have a clear and positive impact upon patient outcome—a fact that fully justifies their use.

## Conclusions

Research in hemodynamic monitorization has been hampered by the fact that discussion has centered more on how than on why. We mix the data supplied by the different systems, some referred to the presence of tissue hypoperfusion, while others inform of the situation of factors determining cardiac function, and upon which we need to act in order to try to correct the previous data. In addition, we use similar intervention protocols in patient groups that differ in terms of either disease or evolutive stage. It is a priority concern to improve the definition of the objectives of resuscitation in our critical patients, depending on type and time. Only in this way will we be able to advance in new measures beyond the mere modification of cardiac yield, and consequently to evaluate those monitorization elements that are best suited to our purpose.

Thus, the impact of hemodynamic monitorization upon the course of the patient depends not only on the reliability of the monitorization systems but also on comprehension of the physiological principles upon which these devices are based, together with strict awareness of their limitations and correct and pondered interpretation of the values obtained. However, in the same way that the most refined Stradivarius, even in expert hands, will sound ordinary and devoid of magic in the absence of an inspired musical score, no hemodynamic monitorization device, however advanced and precise it may be, will exert any positive effect upon the patient outcome unless it is accompanied by a therapeutic protocol of established efficacy.

## Conflicts of interest

M. Ignacio Monge-Garcia serves as a consultant to Edwards Lifesciences. The rest of the authors declare that they have no conflicts of interest.

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