

## EDITORIAL

# Perioperative organ dysfunction: a burden to be countered



## Definition and pathophysiology

In the perioperative setting, organ dysfunction is characterized as an inability of a given organ to perform its functions in a reversible or irreversible manner leading to altered homeostasis requiring clinical interventions or life support to maintain its normal physiology. The development of such complication leads to prolonged hospitalization, increased perioperative morbidity and mortality with short- and long-term consequences having a direct influence on the health-disease process of surgical patients.<sup>1,2</sup> Despite the decrease in anesthesia-related deaths in recent times,<sup>3</sup> deaths related to organ dysfunction in the perioperative period are among the four main causes of death, if they are epidemiologically considered according to the categories reported by the Center for Disease Control. This important clinical issue is ranked just behind cardiovascular diseases, cancer-related deaths and cerebrovascular diseases according to a study published in the American Society of Anesthesiologists (ASA) journal (2). Therefore, the correct identification of patients, who are at higher risk to develop any organ malfunction throughout the perioperative period, is crucial to deliver proper anesthesia care targeting organ protection for better clinical outcomes.

The molecular mechanism of the development of a surgery-related organ dysfunction perioperatively is not completely elucidated. However, pathophysiologically, one of the postulated mechanisms is that its origin could be directly related to uncontrolled inflammation, either of infectious focus like microbial-associated molecular patterns (MAMPs, expressed by pathogens) progressing to sepsis,<sup>4</sup> or a systemic inflammatory syndrome (SIRS) due to excessive production of damage-associated molecular patterns (DAMPs).<sup>5</sup> Both pathways activate immune mechanisms mediated by Toll-like receptors (TLRs), major pattern recognition receptors (PRRs), releasing diverse pro-inflammatory cytokines, chemokines, interferons and reactive oxygen, and nitrogen species, propagating uncontrolled systemic inflammation in individuals genetically prone. This

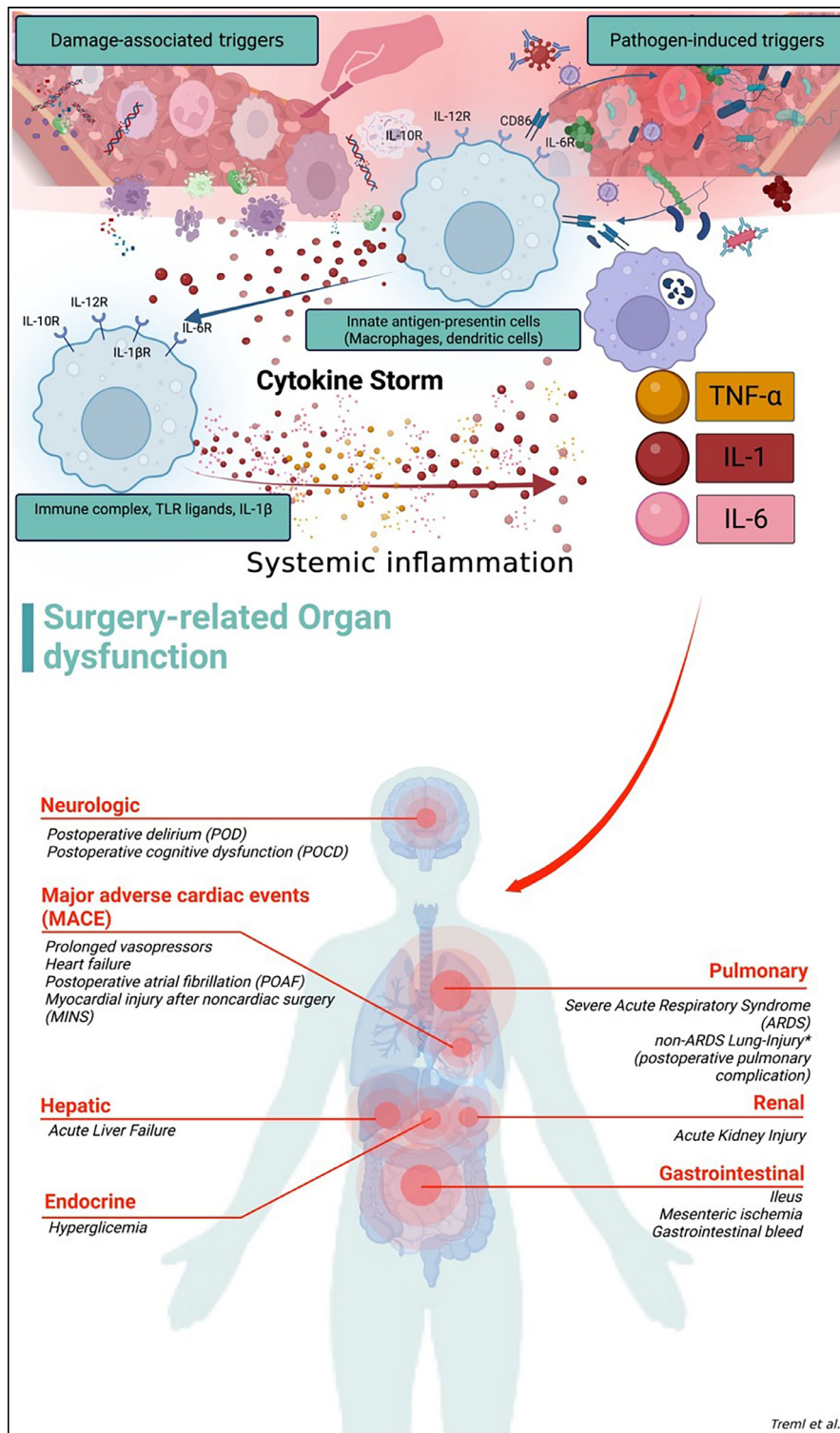
uninhibited inflammation will result in vascular damage, endothelial dysfunction, tissue malperfusion, mitochondrial dysfunction and as a final consequence irreversible cell damage leading to organ dysfunction.<sup>5</sup> The most frequent surgery-related organ dysfunctions are summarized in [Figure 1](#).

## Brazilian scenario

The Brazilian epidemiology of perioperative mortality resembles the international trend of developed and non-developed countries.<sup>3</sup> Since 2008 with the first epidemiological study<sup>6</sup> in high-risk patients evaluating the development of perioperative complications in non-cardiac surgery, the Brasis study<sup>7</sup> in 2020, a significant reduction in mortality has been showed, although they assess different perioperative mortality endpoints ([Fig. 2](#)). This reduction may reflect the introduction of new protocols of multidisciplinary multimodal perioperative care optimization which aimed to establish improvements in perioperative care in Brazil.<sup>8</sup> However, when the incidence of the composite of postoperative complications is analyzed, a marginal progress can be seen in reducing major perioperative complications, which are mainly surgery-related organ dysfunctions. This fact is comparable to the international literature, especially American and European, in which during the past years it has also slowly decreased.<sup>2,9,10</sup> The main organ dysfunctions in both Brazilian studies were cardiovascular, followed by neurological and renal. Abdominal surgery accounted for the highest incidence of complications in both studies. Some independent risk factors were advanced age, emergency and urgent surgery, preoperative anemia, intraoperative transfusion, higher intraoperative fluid balance and high preoperative sequential organ failure assessment score (SOFA) and simplified acute physiology score (SAPS) scores.<sup>6,7,11</sup> Interestingly, even in low-risk patients, perioperative complications were present in significant numbers, with cardiovascular dysfunction accounting for 5.3% of them. This shows the importance of surveillance and preventive efforts even in this low-risk

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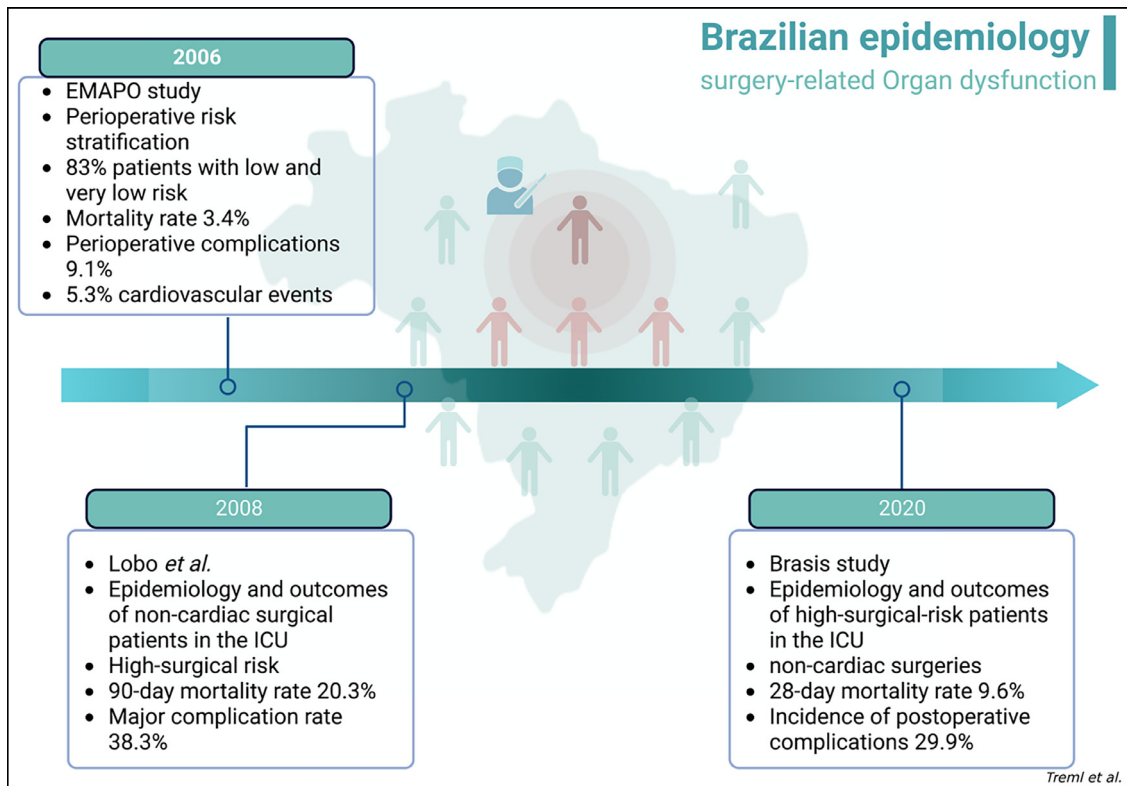
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**Figure 1** The most frequent organ dysfunctions encountered in the perioperative period. \* non-ARDS lung injury, prolonged need for supplemental oxygen, atelectasis, pleural effusion, pneumonia, and reintubation; ARDS, severe acute respiratory syndrome; MINS, myocardial injury after noncardiac surgery; POD, postoperative delirium; POCD, postoperative cognitive dysfunction; POAF, postoperative atrial fibrillation. All images were created with BioRender.com by Ricardo Esper Treml using Academic License Terms.

patient population. Nonetheless, some methodological points of these studies limit generalization of the data for the entire country and for all profiles of patients undergoing different surgeries in Brazil.

First, geographically, more than half of the derived data from these studies are from southwest and south regions, hence, making the correct evaluation and comparison between central, north, and northwest regions difficult.



**Figure 2** Dynamics of Brazilian epidemiology regarding mortality and incidence of perioperative complications. EMAPO, Multicenter study of perioperative evaluation for non-cardiac surgeries in Brazil (EMAPO);<sup>14</sup> Brasis: Epidemiology and outcome of high-surgical-risk patients admitted to an intensive care unit in Brazil.<sup>15</sup> All images were created with BioRender.com by Ricardo Esper Tremi using Academic License Terms.

Second, the core of the data comes from high-risk patients in non-cardiac surgeries, which makes a general assessment difficult in other populations such as cardiac surgery, pediatrics, and obstetric surgery. Ultimately, a direct evaluation and comparison of incidences in the Brazilian private and public sectors is necessary and has not been directly questioned in these studies. Regarding cardiac surgery and perioperative organ dysfunction, a recently published multicenter prospective observational study by Palomba et al has shown in patients receiving coronary artery bypass graft surgery (CABG) under cardiopulmonary bypass a high incidence of cardiac surgery-associated acute kidney injury (CSA-AKI) in both studied groups. Moreover, this study also showed that fluid overload intraoperatively is associated with increased risk in hospital mortality and cardiovascular complications.<sup>12</sup> A more comprehensive view at the incidence of organ dysfunction in other types of cardiac surgery and its associations with clinical outcomes is needed to better understand the Brazilian scenario in this specialty.

### Impact of surgery-related organ dysfunction in clinical outcomes

As previously mentioned, the development of any organ dysfunction during the perioperative period is directly associated with worse clinical outcomes translated as prolonged


stay in the intensive care unit and hospital, higher risk of surgical infection, and increased mortality.<sup>13</sup> The relationship between outcome and organ dysfunction varies greatly depending on the type of malfunction and surgery assessed. One example is the increased risk of death by 1.6 in patients undergoing hip surgery, with the development of postoperative delirium (POD).<sup>13</sup> In addition, the development of myocardial injury after noncardiac surgery (MINS) is strongly associated with 30-day mortality.<sup>13</sup> Even simple hyperglycemia is related to increased risk of infections and perioperative mortality.<sup>1,13</sup> Therefore, taking all these points into consideration, constant vigilance during the perioperative period is of paramount importance. Starting from the detection of patients at risk of developing surgery-related organ dysfunction in the preoperative period, as well as anesthesia planning and implementation of this intraoperatively, to optimization of therapy care postoperatively, the central point is the integral and complete transfer of the patient's clinical information to ensure the absence of gaps in the delivery of clinical treatment. To achieve this, a multimodal and multidisciplinary approach involving all specialties related to the case is essential to deliver the best patient centered anesthesia care.

### Conflicts of interest

The authors declare no conflict of interest.

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