



## Physical fitness and physical function in survivors of sepsis after hospital discharge

*Aptidão física e capacidade funcional em sobreviventes à sepse após a alta hospitalar*

*Aptitud física y capacidad funcional en sobrevivientes a la sepsis después del alta hospitalaria*

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### Abstract

**Introduction:** Severe sepsis may be accompanied by long-term sequelae, and physical aspects related to physical fitness and physical function of sepsis survivors after discharge are still poorly explored. **Objective:** This is an integrative review aimed at analyzing if sepsis survivors present impairment of the physical fitness components and/or physical conditioning and physical function after hospital discharge. **Methods:** The search

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was performed in six electronic databases: LILACS, PubMed, CINAHL, Cochrane Library, Web of Science and Scopus. Controlled descriptors (Sepsis, Septic Shock, Physical Fitness and Activities of Daily Living) and uncontrolled descriptors or keywords (Severe Sepsis, Physical Function, and Physical Status) were used. **Results:** The search resulted in a total of 434 articles, of which seven were eligible for analysis. Of these, none applied a specific physical test to assess the components of physical fitness. Regarding physical function, it was verified that four studies applied specific tests to evaluate the activities of daily living. However, it was observed in most of the studies that the physical aspects were only subjectively assessed through health-related quality of life questionnaires. Overall, all studies analyzed showed that the health-related quality of life of sepsis survivors may be impaired after long periods of hospital discharge. **Conclusion:** Most sepsis survivors presented impairments related to physical fitness and physical function after hospital discharge, as they showed impairments in their functional autonomy, resulting in loss of independence and autonomy in performing the activities of daily living.

**Keywords:** Sepsis. Septic Shock. Physical Fitness. Activities of Daily Living.

### Resumo

**Introdução:** A sepse grave pode ser acompanhada por sequelas em longo prazo, e os aspectos físicos relacionados à aptidão física e à capacidade funcional dos sobreviventes a sepse após a alta hospitalar ainda continuam pouco explorados. **Objetivo:** Trata-se de uma revisão integrativa com o objetivo de analisar se os sobreviventes à sepse apresentam prejuízo dos componentes da aptidão física e/ou do condicionamento físico, e da capacidade funcional após a alta hospitalar. **Métodos:** A busca foi realizada em seis bases de dados eletrônicas: LILACS, PubMed, CINAHL, Biblioteca Cochrane, Web of Science e Scopus. Foram utilizados descritores controlados (Sepsis, Septic Shock, Physical Fitness e Activities of Daily Living) e descritores não controlados ou palavras-chave (Severe Sepsis, Physical Function, e Physical Status). **Resultados:** A busca resultou em um total de 434 artigos, sendo sete elegíveis para análise. Destes, nenhum aplicou um teste físico específico para avaliar os componentes da aptidão física. Em relação à capacidade funcional, verificou-se que quatro estudos aplicaram testes específicos para avaliar as atividades da vida diária. No entanto, observou-se na maioria dos estudos que os aspectos físicos somente foram avaliados de forma subjetiva por meio dos questionários de qualidade de vida relacionados à saúde. No geral, todos os estudos analisados mostraram que a qualidade de vida relacionada à saúde dos sobreviventes à sepse pode estar comprometida após longos períodos após a alta hospitalar. **Conclusão:** A maioria dos sobreviventes à sepse apresentou limitações relacionadas à aptidão física e a capacidade funcional após a alta hospitalar, pois mostraram limitações na sua autonomia funcional, resultando em perda da independência e autonomia em realizar as atividades da vida diária.

**Palavras-chave:** Sepse. Choque Séptico. Aptidão Física. Atividades Cotidianas.

### Resumen

**Introducción:** La sepsis grave puede ser acompañada por secuelas a largo plazo, y los aspectos físicos relacionados con la aptitud física y la capacidad funcional de los sobrevivientes a la sepsis después del alta hospitalaria todavía siguen poco explorados. **Objetivo:** Se trata de una revisión integrativa que objetivó analizar si los sobrevivientes a la sepsis presentan perjuicio de los componentes de la aptitud física y/o del acondicionamiento físico, y de la capacidad funcional después del alta hospitalaria. **Métodos:** La búsqueda fue realizada en seis bases de datos electrónicas: LILACS, PubMed, CINAHL, Biblioteca Cochrane, Web of Science y Scopus. Se utilizaron descriptores controlados (Sepsis, Septic Shock, Physical Fitness y Activities of Daily Living) y descriptores no controlados o palabras-clave (Severe Sepsis, Physical Function, y Physical Status). **Resultados:** La búsqueda resultó en un total de 434 artículos, siendo siete elegibles para análisis. De éstos, ninguno aplicó una prueba física específica para evaluar los componentes de la aptitud física. En cuanto a la capacidad funcional, se verificó que cuatro estudios aplicaron pruebas específicas para evaluar las actividades

de la vida diaria. Sin embargo, se observó en la mayoría de los estudios que los aspectos físicos sólo fueron evaluados de forma subjetiva por medio de cuestionarios de calidad de vida relacionados a la salud. En general, todos los estudios analizados mostraron que la calidad de vida relacionada a la salud de los sobrevivientes a la sepsis puede estar comprometida por largos períodos después del alta hospitalaria. **Conclusión:** La mayoría de los sobrevivientes a la sepsis presentó limitaciones relacionadas con la aptitud física y la capacidad funcional después del alta hospitalaria, pues mostraron limitaciones en su autonomía funcional, resultando en pérdida de la independencia y autonomía en realizar las actividades de la vida diaria.

**Palabras clave:** Sepsis. Choque séptico. Aptitud Física. Actividades cotidianas.

## Introduction

Sepsis is defined as an exacerbated systemic inflammatory response, usually triggered by the presence of bacteria, viruses, fungi or parasites and it is shown with different levels of severity depending on the characteristics of the patient and the time elapsed since their initial clinical manifestations. Sepsis is related to situations in which the Systemic Inflammatory Response Syndrome (SIRS) develops, which may be characterized by a nonspecific response of the organism to a variety of situations that generate inflammation (infection, burns, acute pancreatitis, trauma, among others), usually triggered by infection by invading agents. When sepsis progresses to dysfunction of one or more organs it is called severe sepsis and septic shock if there is hypotension that does not respond to aggressive fluid replacement, thus needing administration of vasoactive agents to maintain blood pressure at compatible levels with life. The latter condition is notably a marker of poor prognosis, significantly interfering with the outcome of patients with infection [1]. Sepsis and severe sepsis are the leading causes of death in the United States and the most common cause of death among critically ill patients in intensive care units (ICUs) [2, 3].

In Brazil, the Brazilian Sepsis Epidemiological Study (BASES study) showed a general mortality of 21.8% in up to 28 days of hospitalization, and among the 1,383 patients analyzed, the incidence of sepsis, severe sepsis and septic shock was 61.4; 35.6 and 30.0 per 1,000 patients per day, respectively [4]. In another study, a general mortality rate of approximately 46.6% was observed in the short term, and when the subgroups sepsis, severe sepsis and septic shock were observed, mortality was 16.7%, 34.4% and 65.3%, respectively [5].

Severe sepsis is often associated with multiple organ failure, and although not accurately understood, it is known that the exacerbated inflammatory process can alter peripheral metabolism, coagulation, and hemodynamic stability leading to organ failure or death. In addition, the high lethality of sepsis is not restricted only to the acute phase of the disease, since it also increases the risk of death in the years following hospital discharge [6, 7]. Thus, monitoring the long-term sequelae of sepsis survivors has become a major concern among health professionals and clinical investigators, and some studies indicate that these sequelae may result in a significant reduction in health-related quality of life (HRQL) of these people [8, 9]. However, there are indications that the reduction in HRQL is not different from that in other critical conditions without sepsis [10].

In addition to HRQL, sepsis may also affect the physical fitness of survivors. Being physically fit consists of the ability to perform daily tasks with vigor and agility, without undue fatigue and with sufficient energy to enjoy leisure activities and to respond to unforeseen emergency situations [11]. Physical fitness has a performance-related and a health-related component, and the latter is considered more important for public health, since it includes cardiorespiratory fitness, resistance training, muscle strength, flexibility and body composition [11, 12].

Physical function, on the other hand, implies the ability to perform activities that allow the individual to take care of himself and live independently [13]. Several studies have pointed out that survivors of sepsis may experience functional impairment in the long term and suggest that investigations related to subjects who have been admitted to the ICU should include a follow-up aimed at improving the patient's quality of life and physical condition [14, 15], that is, it should also aim at improving the physical conditioning of sepsis

survivors, with a view to their rehabilitation in order to carry out the activities of daily living independently. However, the magnitude of the functional impairments of sepsis survivors is still unknown, and it has been hypothesized that many of these survivors who have spent time in the ICU have numerous cognitive and functional impairments after hospital discharge [16].

Although the literature presents several studies that have explored the effect of sepsis on HRQL, there is a shortage of studies related to the assessment of physical fitness and physical function of these patients. So, this integrative review aimed to analyze if sepsis survivors present impairment of the physical fitness components and/or physical conditioning, and physical function after hospital discharge.

## Methods

This integrative review was carried out in six stages: identification of the theme and the research question; establishment of criteria for inclusion and exclusion of studies and search in the literature; definition of the information to be extracted from the selected studies and categorization of the studies; evaluation of studies included in the integrative review; interpretation of the results and presentation of the knowledge synthesis [17].

The guiding question for this review was: "Do survivors of sepsis present impairment of the physical fitness components and/or physical conditioning and physical function after hospital discharge?" The search for electronic databases took place in November 2014, and six databases were consulted, such as the Latin American and Caribbean Literature in Health Sciences (LILACS), the US National Library of Medicine, National Institutes of Health (PubMed), CINAHL, Cochrane Library, Web of Science and Scopus.

Controlled descriptors extracted from the Descriptors in Health Sciences (DeCS) and the Medical Subject Headings (MeSH) were used, in addition to uncontrolled descriptors. Boolean operators "AND", "OR", and "AND NOT" were used in all crossings. The controlled descriptors used were Sepsis, Septic Shock, Physical Fitness and Activities of Daily Living, and the uncontrolled descriptors or keywords used were: Severe Sepsis, Physical Function, and Physical Status.

The inclusion criteria were original articles that addressed the physical function and physical fitness of patients who survived an episode of sepsis, severe sepsis and septic shock, published in English, Spanish, French

and Portuguese periodicals and without delimitation of the period of publication. Exclusion criteria were: studies conducted with subjects younger than 18 years or assessing the effect of a sepsis episode in childhood for comparison with physical function and physical fitness in the adult, publications that evaluated the effects of specific treatments for sepsis compared to the standard treatment for subsequent evaluation of physical function and physical fitness, publications that were not included in the classification of the level of evidence used [18], animal studies, editorials, letter to the editor, dissertations, theses, literature reviews, and articles without abstracts that did not have text available.

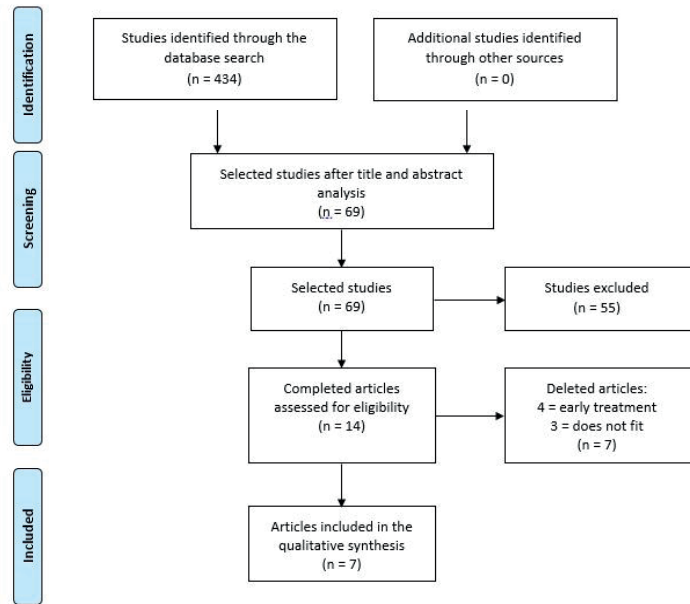
For the extraction of the data obtained from the articles analyzed, a validated instrument was adapted, which includes the identification of the article, the authors, the type of publication, the methodological design, the sample design, the studied intervention, the results, and conclusions [19]. The selected publications were classified according to the methodological design and level of evidence, and the synthesis of the data is presented in a descriptive way.

## Results

In the initial search, 434 articles were identified, of which 69 were selected after the title and abstract analysis. Of these, 34 were repeated and 21 did not meet the inclusion criteria. So, 14 articles were selected for the complete reading and seven were eligible for analysis. Of the seven articles that were excluded after reading the full text, three did not meet the inclusion criteria and four were related to functional electrical stimulation (FES) in the ICU, that is, they were related to early treatment. The details of the selection of articles are presented in Figure 1.

The publications found were published between 2000 and 2013, with most studies categorized as prospective longitudinal, with level of evidence IV [18]. Regarding the language of publication, eight articles were published in English and one in Portuguese. Regarding the design, two studies were prospective cohort, two were cross-sectional, four were longitudinal, and one comprised a prospective cohort and a cross-sectional study.

Four studies were carried out in Europe, three in North America, one in Asia, and only one was developed in South America. Table 1 presents the objectives of the studies and the instruments used. Table 2 summarizes the articles included in this integrative review, according to the main results and conclusions.



**Figure 1** - Flowchart of the analyzed studies.

Note: Adapted from: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *Ann. Intern. Med.* 151(4): 264-269 [20].

**Table 1** - Synthesis of studies according to objectives and instruments used

(To be continued)

Authors	Objective	Tools used
Zhang et al., 2013. [21]	To systematically evaluate HRQL and job in survivors of severe sepsis, up to six years after hospital discharge.	<ul style="list-style-type: none"> <li>• SF-36</li> <li>• Instrumental Activities of Daily Living.</li> </ul>
Westphal et al., 2012. [22]	To describe the repercussion of severe sepsis and septic shock on quality of life after hospital discharge.	<ul style="list-style-type: none"> <li>• SF-36.</li> </ul>
Meurer et al., 2011. [23]	To assess the degree of functional decline and loss of independence among the elderly patients seen in the emergency department with severe infection and estimate the mortality up to 90 days after hospital discharge.	<ul style="list-style-type: none"> <li>• Index of Activities of Daily Living</li> <li>• Instrumental Activities of Daily Living.</li> </ul>

(Conclusion)

Iwashyna et al., 2010. [24]	To determine the change in cognitive impairment and physical function among patients who survive severe sepsis, controlled by their pre-sepsis functioning.	<ul style="list-style-type: none"> <li>• Index of Activities of Daily Living</li> <li>• Instrumental Activities of Daily Living</li> <li>• Informant Questionnaire on Cognitive Decline of the Elderly (IQCODE).</li> </ul>
Poulsen et al., 2009. [25]	To evaluate the physical recovery of survivors of septic shock one year after hospital discharge.	<ul style="list-style-type: none"> <li>• SF-36</li> <li>• Questionnaire for evaluation of self-perceived physical function.</li> </ul>
Hofhuis et al., 2008. [26]	1 - Describe the impact of severe sepsis on HRQL in patients with severe sepsis during ICU and hospital stay and up to six months after discharge from ICU using SF-36. 2 - To compare HRQL at admission and six months after ICU discharge from survivors of severe sepsis with that of the Dutch population in general.	<ul style="list-style-type: none"> <li>• SF-36.</li> </ul>
Heyland et al., 2000. [8]	To describe the long-term HRQL of sepsis survivors and to evaluate the reliability and validity of the Medical Outcomes Study Short Form-36 (SF-36) in this population.	<ul style="list-style-type: none"> <li>• SF-36</li> <li>• Patrick's Perceived Quality of Life Scale (PQOL).</li> </ul>

Note: HRQL = Health-related quality of life; SF-36 = Short-Form 36 health survey; ICU = Intensive care unit.

**Table 2** - Synthesis of the studies, according to the main results and conclusion

(To be continued)

References	Results and Conclusions
Zhang et al., 2013. [21]	<ul style="list-style-type: none"> <li>Regarding physical function assessed by the SF-36, the mean between the sepsis group and the critical controls was <math>79.12 \pm 21.22</math> vs <math>83.18 \pm 27.30</math>, respectively.</li> <li>Regarding activities of daily living, 33 (78.6%) of those interviewed with severe sepsis and 26 (78.8%) of those with critical illness had no complaints about their physical condition, or had only minor complaints. Nine patients with severe sepsis and seven critical controls had a major functional impairment. At the time of the interview, 71.1% of patients who had severe sepsis and 76.7% of those with critical illness had returned to work. Conclusion: Survivors of severe sepsis still had their health-related quality of life impaired, even up to six years after hospital discharge.</li> </ul>
Westphal et al., 2012. [22]	<ul style="list-style-type: none"> <li>There was impairment in the survivors compared to the control group on SF-36 domains related to Physical Function (<math>59 \pm 32</math> versus <math>91 \pm 18</math>, <math>P &lt; 0.001</math>) and Physical Aspects (<math>60 \pm 45</math> versus <math>87 \pm 34</math>, <math>P &lt; 0.02</math>), respectively. In addition, they obtained lower scores than controls in the summary of Physical Health (<math>62 \pm 20</math> versus <math>78 \pm 12</math>; <math>P &lt; 0.004</math>), respectively. Conclusion: Severe sepsis may result in a significant impairment of the health-related quality of life of those surviving hospitalization, as well as compromising the likelihood of long-term survival.</li> </ul>
Meurer et al., 2011. [23]	<ul style="list-style-type: none"> <li>Impaired physical function was initially more severe in patients with suspected sepsis than in controls (<math>P &lt; 0.01</math> for each activity).</li> <li>There were no detectable differences in the degree of impaired physical function of patients with sepsis at follow-up, and interestingly, eight of 34 (23.5%) patients had an improvement in function level in one or more activities compared to their performance in the onset of the acute disease. The differences assessed at hospitalization and after 90 days were not significant in either cases or controls.</li> <li>Patients from households had a lower risk of functional decline than those from care facilities.</li> <li>None of the patients experienced an increase in residential independence after hospital discharge; and eight of the 19 survivors (42.1%) required care or had moved to a care facility 90 day after their hospitalization. Conclusion: Although functional status does not consistently deteriorate in sepsis survivors, there is a considerable risk of loss of independence in the short term when evaluated in their homes.</li> </ul>
Iwashyna et al., 2010. [24]	<ul style="list-style-type: none"> <li>High rates of new functional impairments were seen after sepsis: in those without impairments before sepsis, an average increase of 1.57 new impairments occurred (95% CI: 0.99 - 2.15); and for those with mild to moderate impairments before sepsis, an average increase of 1.50 new impairments was observed (95% CI 0.87 - 2.12). The decline in cognitive and physical function persisted for at least eight years. Conclusion: Severe sepsis in the elderly population was associated with substantial and persistent cognitive impairment and functional disability among survivors. The magnitude of these deficits was large, resulting in the inability of these people to live independently.</li> </ul>
Poulsen et al., 2009. [25]	<ul style="list-style-type: none"> <li>Scores for domains related to physical health were severely reduced in patients with septic shock compared to the equivalent control group at age and sex.</li> <li>Scores for the physical function domain were also reduced among patients with septic shock compared to the control group (<math>65</math> vs <math>90</math>, <math>P &lt; 0.0001</math>).</li> <li>Twelve months after discharge, two-thirds of patients (47/70) reported a significant deterioration of physical function compared to pre-hospitalization status. 81% (38/47) of the patients attributed the decrease in physical fitness to loss of muscle mass.</li> <li>Only 43% (10 vs 23, <math>P = 0.01</math>) of septic shock survivors who had permanent employment prior to admission had returned to work. Conclusion: Physical conditioning was substantially reduced in septic shock survivors one year after hospital discharge.</li> </ul>
Hofhuis et al., 2008. [26]	<ul style="list-style-type: none"> <li>Six months after ICU discharge, scores for the physical function, physical aspects and general health status domains were still significantly lower than pre-admission values (all <math>P &lt; 0.05</math>).</li> <li>In addition, scores were lower than those of the population in the domains of emotional aspects, physical function, general health status, vitality, mental health and physical aspects (all <math>P &lt; 0.01</math>).</li> <li>Conclusion: Despite they showed a gradual improvement during the six months after ICU discharge, recovery was incomplete in the physical function, physical aspects, and general health status six months after ICU discharge compared with pre-admission status.</li> </ul>
Heyland et al., 2000. [8]	<ul style="list-style-type: none"> <li>Sepsis survivor scores were significantly lower on the domains of physical function, physical aspects, general health status, vitality, and social aspects, as well as in the summary of overall physical health when compared to the general US population.</li> <li>Regarding the physical function domain, the study showed that the mean among patients with sepsis compared with the US population was <math>48.3</math> (32.7) vs <math>72.3</math> (23.3), respectively. Conclusion: The long-term health-related quality of life of sepsis survivors is significantly lower than that of the general US population. The SF-36 demonstrated good reliability and validity when used to assess health-related quality of life in sepsis survivors.</li> </ul>

Note: SF-36 = Short-Form 36 health survey; EQ-5D = EuroQoL-5D; ICU = Intensive care unit; RMI = Rivermead Mobility Index; USA = United States of America; CI = confidence interval; vs = versus; Continuous variables are expressed as average  $\pm$  standard deviation.

## Discussion

This integrative review on physical fitness and/or physical conditioning and physical function in sepsis survivors showed that survivors may present impairments related to the physical fitness components and/or physical conditioning and physical function after hospital discharge, resulting in loss of independence and autonomy in carrying out the activities of daily living [8, 21].

Although the aim of this review was not to evaluate HRQL, some studies have shown that the HRQL of patients who had experienced a severe sepsis episode have improved over the years, the recovery of physical fitness components and/or physical conditioning and physical function is not complete and may interfere significantly in the HRQL of these subjects [8, 27, 28]. In this review, all studies analyzed showed that the HRQL of sepsis survivors may still be impaired in the long-term [8, 21].

There was also a high mortality after hospital discharge, mainly among the elderly. An earlier study showed that mortality remained elevated during the first year after sepsis, and that the increased risk of death persisted for up to five years after hospitalization. The life of a patient who survives a sepsis episode may be reduced by 2.6 years [7].

One of the great difficulties in the development of this review was to find studies in which physical tests were performed on survivors of sepsis to assess physical fitness and/or physical conditioning. In the studies analyzed, none of these tests were performed. The interest in studies in which physical tests were performed was to find results in which physical conditioning and performance-related or health-related physical fitness components had been specifically assessed in these subjects. Performance-related physical fitness components include skills such as agility, balance, coordination, speed, power, and reaction times [11, 29]. The health-related physical fitness components include cardiorespiratory fitness, resistance training, muscle strength, flexibility and body composition [11, 12, 29].

A study that evaluated the functional evolution of intensive care patients with polyneuropathy, six and 12 months after diagnosis of the critical illness, but which included in its results some patients with sepsis, performed a test to assess physical fitness and/or physical conditioning, which consisted of the Up and Go walking test [30]. The evaluation of these parameters is important, since the decrease in muscle strength can result in problems for the practice of physical activities, to go up and down stairs, and in carrying out activities like

picking up objects from the ground, considering that the impairment in muscle strength and/or cardiorespiratory fitness may have limited the performance of activities of daily living [30]. Other factors may also have influenced sequelae in survivors. In the literature, the severity of the disease, the occurrence of multiple organ dysfunction, pre-hospitalization functional dependence, age and diagnosis at admission are described as determinants of patient outcome related to physical aspects after prolonged ICU stay [31, 32]. However, it is still unclear whether these factors contribute to a decrease in physical health and a small improvement in physical function in the long-term [28].

Another factor that may also contribute to the decrease of the physical fitness components and/or physical conditioning in patients who have undergone prolonged ICU hospitalization are weakness and loss of muscle mass due to prolonged rest and immobility [33, 34]. Muscle weakness occurs early during critical illness and is more severe in patients who have had multiple organ dysfunctions than in patients who have had dysfunction in a single organ. The loss of muscle mass is largely due to decreased protein synthesis; however, several modifiable and non-modifiable factors influence the loss of muscle mass [35, 36].

The literature on ICU care suggests that hospitalized patients may acquire weakness, chronic myopathy and polyneuropathy, and suggest that there is direct inflammation in the muscle and hypo perfusion mediated by degradation of muscle fibers and neurons [37] that may be exacerbated by prolonged immobility [34, 38] and lack of adequate physiotherapy [39]. Thus, there are plausible multiple causal pathways by which sepsis and its treatment can lead to significant declines in physical function.

Regarding physical function, it implies the ability to perform activities that allow the subject to take care of himself and live independently [13]. It is usually analyzed using standardized instruments assessing the performance in activities of daily living and instrumental activities of daily living [40, 41]. It was verified in this review that four studies applied tests in which activities of daily living were evaluated [21, 23-25]. However, it has been observed in most studies that physical aspects were only subjectively assessed through quality of life questionnaires.

Some studies that did not emphasize the episode of sepsis, but that assessed the physical function of elderly patients who have gone through a period of hospitalization, observed a decline in physical function along with an increase in mortality [42 - 44]. A study

that assessed the functional status of the elderly 12 months after discharge from the ICU, observed a significant decrease in functional autonomy. However, it was not possible to assess physical function results in sepsis survivors, since the study described the number of patients with sepsis who were found, but the results for physical function analysis were not described for the population with sepsis, and yes for all the elderly assessed [42].

In recent studies, the authors emphasized the importance of early and intensive rehabilitation with patients still hospitalized in the ICU through FES to reduce residual deficits related to physical function and shorten the rehabilitation process [45, 46].

The primary outcomes expected for the patient are improvement or maintenance of strength and physical function. The evaluation of an early rehabilitation program involving the FES combined with adapted cycling, which can be initiated at the critical period, in which most of the muscle mass decreases occur, can provide directions for the development of proper rehabilitation to patients from the ICU [45]. In this study, the authors also assessed the safety and viability of the FES combined with cycling and compared the controls in terms of functional recovery and evolution of delirium and found that the use of FES associated with cycling is safe and feasible, and preliminary results suggested that this association can improve mobility and decrease patient delusions. However, further research is needed to confirm the results of the study and to assess the efficacy of FES associated with cycling [46]. Other studies also encouraged early physical rehabilitation during hospitalization through physical therapy [34, 47 - 50], as well as neuromuscular electrical stimulation, which has been shown to be safe and effective [51 - 54], but also describe that further study is necessary.

An important aspect that has also been observed in survivors of sepsis is that the direct costs, which are those related with treatment in general, are higher in the years following hospitalization [55]. Indirect costs, which make up about 70% of the total cost, are related to the abbreviation of the productive years of life due to the high mortality and the decrease of the HRQL [7, 56]. In addition, many patients report that because of their decreased physical fitness and/or physical conditioning, they cannot get back to work and do it as the way it was before the illness [21, 22]. Some studies have observed that only half of the patients who were admitted to the ICU returned to work one year after hospital discharge [57, 58].

Some studies show that the systematization of therapeutic regimens may help reduce mortality and the direct hospital cost related to sepsis [2, 59, 60].

Thus, it is believed that with the adoption of rehabilitation and reintegration programs for these subjects, it might be possible to accelerate the recovery of productive capacity and reduce the indirect cost of sepsis to society [22]. Sepsis survivors' complications are a substantial public health problem with important implications for patients, families and the health system [24].

## Conclusion

This review showed that most survivors of sepsis presented impairments related to physical fitness and/or physical conditioning and physical function after hospital discharge, as they showed impairments in their functional autonomy, resulting in loss of independence and autonomy in carrying out the activities of daily living. Thus, the adoption of early rehabilitation programs for patients who had experienced an episode of sepsis and were admitted to the ICU, and the long-term follow-up of these subjects may help their return to a healthy and independent life.

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