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Chronic Pain in Intensive Care Survivors

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Abstract

Intensive Care focus has shifted over the last decades, establishing the importance of patients' prognosis and quality of life, not only patient survival. As such, several studies have been conducted recently to evaluate patients outcome and quality of life after Intesive Care Unit (ICU) discharge identifying several long term sequels in critical patients. Of those, chronic pain is one of the most commonly identified physical impairments found in critical patients, with a 6 months after discharge prevalence of 22 to 44%. This literary review aims to resume the prevalence, characteristics, risk factors of chronic pain and its impact on health-related quality of life in intensive care survivors.

Studies included in this review were obtained from an online database advanced search. Only publications after January 1, 2000 were considered. A total of 12 articles were included in this literature review from several nationalities.

Patients with chronic intensive care-related pain (CIRP) report high pain intensities and high burden of pain compromising their normal daily life and activities. Effectively, patients with CIRP report significantly lower quality of life than critical patients without chronic pain. Several risk factors for the development of chronic pain were presented, such as sepsis, severity of illness, pre-existing chronic pain, among others. With this review it is evident the need for further investigation in order to better understand this entity for more effectively patient care and management.

Keywords

Chronic pain; critical care; intensive care; persistent pain; risk factors;

Abbreviations list

ICU – intensive care unit

PICS – post intensive care pain

CIRP- chronic intensive care-related pain

HR-QoL - Health-related quality of life

BPI – Brief pain inventory

EQ-5D - EuroQol five-dimensions

SF-36 - 36-item short form health survey

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Introduction

During the poliomyelitis pandemic , in 1953, the concept of ICU was created as a special unit to provide multidisciplinary care to patients with respiratory failure.[1] The World Federation of Societies of Intensive and Critical Care Medicine defines ICUs as "an organized system for the provision of care to critically ill patients that provides intensive and specialized medical and nursing care, an enhanced capacity for monitoring, and multiple modalities of physiologic organ support to sustain life during a period of life-threatening organ system insufficiency".[2]

Today ICUs are reserved to patient in need of critical care and life support. Most commonly critical care is reserved to patients with severe organ disfunction, major trauma or intervention. In developed countries, ICU mortality rates range from 16,5 to 32,5%.[3]

Over the last two decades the utilization of critical care units has increased significantly, both due to aging population and their associated comorbilities. Nonetheless, despite the increasing number of critical patients, there has been a decrease in the mortality, resulting in a growing number of ICU survivors. In the US, a study involving ICU patients from 1998 to 2012, showed a reduction in 35% of the mortality, despite of the increasing age as well as severity of illness of the patients admitted.[4]

Mortality risk for a patient after ICU discharge remains higher than for general population for several years, with Brinkman et. al, showing it was 12.5%, 19.3%, and 27.5%, 1, 2, and 3 years after hospital discharge respectively (vs general population in study was 2,4%, 5,1% and 8,2%).[5] Those levels of mortality should encourage more research in order to further improve the odds for these critically ill patients. However, more than battling against mortality rates in these severe ill patients, it is important to realize the morbidities they have to face after their discharge.

This represents a shift in the focus of intensive care over the last decades, establishing the importance of patient´s quality of life and morbidity evaluation, besides patient´s survival. In the past, limited attention had been placed on the long term complications of critical care, with mortality or survival rates being the dominant outcome measurements in research for years.[6]

Therefore, recently several studies have been conducted to evaluate patient's outcome and quality of life after a period in the ICU, in order to help and guide health professionals in the challenge of preventing and managing the long-term complications of critical care.

Survivors of critical illness are frequently left with variety of physical and psychological long term impairments, recently described as post intensive care syndrome (PICS). [7] This can include a wide range of symptoms such as chronic pain and weakness, sleep deprivation, fatigue, which might appear alone or in combination, as well as anxiety, depression post-traumatic stress disorder or a decline in cognitive functions like memory, mental processing speed and executive functioning.[8]

These changes can persist months or years after ICU discharge and cause a decrement of health-related quality of life (HRQoL) in patients treated in an ICU.[9] Most, if not all patients in intensive care units will experience pain at some point during their ICU stay[10], but perhaps more important a review on this matter reported that this pain commonly persists after discharge.[11] Nociceptive, neuropathic and nociplastic pain can occur in ICU survivors, but there is limited knowledge and information about its aetiology and characteristics. Therefore, the development of chronic pain following ICU care, which can be part of PICS or in isolation, has an important impact in patients quality of life and outcome[12] and is an area on increasing research.

Several definition of chronic pain are used but the essence of all is that it is a persistent pain that continues longer than the normal period of healing. Chronic pain is defined in ICD-11 as persistent or recurrent pain lasting more than 3 months which is associated with significant emotional distress or functional disability.[13] In Europe, chronic pain of moderate to severe intensity occurs in 19% of the adult population.[14] When focusing in patients treated in an hospital ICU, this percentage can be much higher. Estimates of the prevalence of chronic pain in the year after discharge range from 15 to 77%, depending on the type of study, moment and tools used to assess pain. Chronic pain not only has a high incidence but also prevalence in intensive care survivors, in fact a study revealed cases of pain in ICU survivors up to 11 years after discharge.[15] Furthermore, recent studies show patients with chronic intensive care related pain (CIRP) reported significantly lower health-related quality of life than patients admitted to the ICU without CIRP.[16] CIRP was defined as clinical relevant pain 6 months after ICU discharge lasting for at least three to six months and when patients attributed this pain to the ICU stay.[17] Therefore it is clear the major impact chronic pain can have in critical care patients after ICU discharge, making extremely important the identification of predictors of chronic pain and understanding of the pathophysiology behind its origin.

Pain is a subjective complex multidimensional phenomenon, influenced by many physiological, psychological, emotion and social factors. On that grounds, in the recent studies in ICU patients populations are highlighted several risk factors that might be associated with an increased risk of chronic pain after ICU discharge such as pre-existing chronic pain, admission category in the ICU, length of stay in the ICU, number of days on a ventilator or patient's age. [15,18] The identification of these is not only relevant for the understanding of the mechanisms leading to the development of chronic pain, but particularly as possible contributor factors that healthcare professionals can address to reduce the incidence of chronic pain, subsequently increasing the quality of life, in patients after an ICU admission.

The importance of post-intensive care is highlighted with the recent epidemiologic reality. The COVID-19 pandemic lead to an explosive ICU admissions and a change in demographics of the

patients admitted. In fact, we saw a higher amount of younger, without comorbidities, patients facing a new disease with multi-organic disfunction.

Objectives

This thesis aims to provide a literature review of the prevalence, characteristics and risk factors of chronic pain and the impact in the health-related quality of life in intensive care survivors. Chronic pain has a significant impact in the quality of life of patients after ICU discharge and has a higher prevalence than the general population, so research in this topic is not only pertinent to clarify the mechanisms underlying its development but mainly to identify possible areas of intervention in order to improve outcome of intensive care survivors.

Therefore, this literature review will highlight the most pertinent recent studies about chronic pain focusing on its importance in the reduction of patients' quality of life as a consequence of their admission to an intensive care unit.

Methods

The literature search was conducted in several online databases including PubMed, Medline, Science Direct and Google Scholar using the following terms: 'chronic pain' or 'persistent pain' or 'quality of life' and 'critical care' or 'intensive care' or 'critical illness'. Only studies with adults were included as well as publications made in English, Portuguese or Spanish. The database searches were performed on October 18, 2020, January 17, 2021. It was established a time limit, including only studies conducted since January 1, 2000.

Some of the studies included on this review were not specifically about chronic pain in intensive care survivors, but focused on these patient´s quality of life outcomes and pain was one of the evaluated parameters. If a study focusing on critical patients' health related quality of life did not describe the results with a specific category for pain or physical discomfort, it was excluded. A total of 12 articles were included in this literature review from several nationalities. The description of the included studies is presented in Table 1.

Discussion

Incidence/prevalence of chronic pain

Chronic pain incidence or prevalence was accessed in the several studies using different tools, some pain-specific like the Brief Pain Inventory (BPI)[15,19,20] or the German Pain Questionnaire[16,17] and other to assess health-related quality of life (HR-QoL) such as EQ-5D[3,21] or EQ-6D[9] and the 36-item short form health survey (SF-36)[22,23]. A overall summary is presented in table I, including which tool was used in each study.

In the studies considered in this literature review, estimates of the prevalence or incidence of chronic pain after discharge range from 15 to 77%, depending on the type of study, timing of assessment and tool used to evaluate pain.[3,9,15–17,19–24] Results are shown in table II. The highest prevalence of chronic pain was registered by Hayhurst and colleagues, with 77% of the patients reporting persistent pain symptoms 3 months after discharge[20]. At 3 months after ICU discharge the percentage of patients with chronic pain ranged from 31 to 77%; at 6 months from 22 to 44% and at 12 months from 15 to 74%. 5 years after discharge, Cutherbertson *et al*, described a pain incidence of 62% (bodily pain).[23]. Timmers *et al*, evaluated ICU survivors pain in a single moment in time, so patient's time after discharge ranged from 6 to 11 years, and even in a such a long interval ICU survivors chronic pain prevalence was 57%.[9]

Pain sites

In the general population chronic pain most prevalent site is the back (42%), but also more than 40% had joint pain, being the knee the most frequent joint affected (16%).[14] In the ICU survivors, the most common chronic pain sites were the shoulder, abdomen and foot/ankle.[15,19] In the study by Battle and colleagues the most frequently reported body part affected was the shoulder (22%).[15] Langerud *et al*, also identifies shoulder/upper arm as one of the most common sites of pain identified by ICU survivors.[19] Both authors agreed that this pain site might occur due to the high amount of invasive equipment placed in this location (for example central lines or dialysis catheters), or due to the techniques used to held patients and move them, or even due to immobility of patients being bedridden for long periods of time.

One year after ICU discharge the most common site of pain referred by Langerud and colleagues was the ankle/foot, and pain in the knees, thighs, neck, hands and head also increased significantly between 3 months and 1 year. In this period the pain prevalence decreased from 49,2 to 38,2% but the median number of sites of pain was 2 at 3 months and increased to 3 at 1 year. The author suggested this findings could be explained by patients' increased mobility and activity levels (at 1

year compared to only 3 months after discharge), justifying pain located in weight bearing joints and muscles. [19]

In this study[19], abdomen was also pointed as a site for high incidence of pain at three months, but this might be a bias due to the large group of abdominal surgery patients present in the sample.

Finally, this study also concluded the most common sites of pain were not linked to the admission diagnosis.[19] Therefore it possible to theorize that the pain site might be associated with the procedures conducted in the ICUs.

Conclusions concerning the pain sites of chronic pain might have some limitations as the majority of the studies did not accessed them. So, further investigation about pain location and its possible association with admissions diagnose is needed.

Risk factors

The incidence of chronic pain in intensive care survivors is high, however the studies present conflicting evidence supporting predisposing risk factors to its development.

Age

Battle *et al* also pointed out increasing age as an independent risk factor for the development of chronic pain.[15] Accordingly, Cuthbertson and colleagues study had physical scores (evaluated using SF-36) significantly lower in older patients in the premorbid period, but there were no significant differences after the ICU stay. These patients have poor pre-morbid physical scores when compared to the general population what suggests these patients have a significant burden of ill-health before critical illness but not necessarily have worst outcomes after discharge due to this. [23] Besides that, other studies suggested lower age might be associated with chronic pain and reduction in patient's quality of life.[16,22] In Boyle *et al*, younger age groups in the study sample demonstrated much greater reduction in HR-QoL, reporting higher physical health disabilities than older age groups.[22] According to the author, older patients' tendency to a more positive view on their life situation may explain these findings. Likewise, Jeitziner *et al* study focused specifically in elderly patients, and the results showed critically ill older patients did not report increased pain, anxiety or agitation one year following an ICU stay. [24] Baumbach and colleagues results showed lower age, female sex and increased levels of anxiety before ICU admission were predictive for chronic intensive care related pain (CIRP).[16] Therefore there is no clear association between older age and chronic pain after intensive care, since evidence is not clear and contradictory.

Admission diagnosis

Finally, neither of the studies revealed the admission diagnosis in the ICU as a potential risk factor for chronic pain after discharge. In fact, Boyle *et al* results show no difference in the incidence of chronic pain amongst patients with different reasons for ICU admission (elective surgery, emergency surgery or medical patients).[22] The results of Jagodic *et al*, of trauma and sepsis ICU patients supports this findings, because there was not a significant difference in terms of the quality of life after 2 years of follow up between the groups.[3]

Sepsis

Sepsis is one of the leading causes of death in critically ill patients and associated with a prolonged stay both in the ICU as in the hospital.[25] Battle and colleagues found that sepsis was a significant independent predictor for the development of chronic pain 6 months after ICU.[15] Hayhurst *et al* findings are consistent with the observations, revealing survivors of sepsis had higher pain scores than their age-matched counterparts.[20] On the contrary, a more recent study of Baumbach *et al* was specifically designed to evaluate the role of severe sepsis and septic shock in chronic intensive care-related pain.[17] Results showed the total prevalence of pain states associated with the ICU stay did not differ between septic and nonseptic patients 6 months after ICU discharge.[17] Backing this results, there is also the study of Granja *et al* in which septic patients although having a greater severity of disease on admission, performed as well as or even better than other ICU survivors, when evaluated 6 months after discharge in terms of health related quality of life.[21] Also, Jagodic *et al* study, which compared the long term and quality of life in sepsis and trauma ICU survivors, revealed that patients with sepsis treated in the surgical ICU have higher short-term (in the ICU and in-hospital) and long-term mortality than trauma patients, but there was not a significant difference in terms of the quality of life after 2 years following intensive care between the sepsis and trauma group.[3] Further investigation is needed to determine whether in fact sepsis does not lead to a higher prevalence of chronic pain in intensive care survivors.

Severeness illness

Langerud *et al* did not confirm any of the possible risk factors previously mentioned (age or sepsis), however the results of this study raised the possibility that the more severe critical illness (ventilator time >12 days, high SAPS II and SOFA score) may predict the risk of developing chronic pain 1 year after discharge.[19] This was not the only study to establish a connection between mechanical ventilation and hospital length of stay with chronic pain after intensive care. Boyle *et al* study demonstrates that each additional 10 ventilation hours and each additional 10 days in the

hospital was associated with an increased risk of chronic pain of 10% and 27%, respectively. In fact, when adjusted for admission category, age and gender, ventilation hours and hospital length of stay were significant predictors of chronic pain.[22] However neither Baumbach and colleagues or Jeitziner *et al* found an association between pain and the duration of ICU stay.[16,24]

Pre-existign chronic pain

Pre-existing chronic pain before ICU admission, apart from what could be excepted, was not a risk factor for chronic pain after ICU discharge according to Battle *et al*.[15] However, in Baumbach *et al* those patients with pre-existing chronic pain reported additional sources of pain after ICU discharge[16], in fact 17% of the patients reported chronic pain conditions prior to ICU admission and reported additional sources of chronic pain after ICU. [17] Jeitzner *et al* study results showed that ICU group patients with pain prior to admission had significantly more pain at 12 months after discharge.[24] In this same study, the results evidenced that surgical procedures during the ICU were significantly associated with more pain directly after discharge.[24] However when talking about surgery itself, it is not a risk factor for chronic intensive care-related pain.[17]

Pain management

Appropriate management of acute pain is suggested to reduce the risk of chronification.[11] Opioids are one of the major pain management therapies used in these units. Recent studies have suggested that the use of opioids may contribute to opioid-induced hyperalgesia and/or the development of chronic pain. [26] However none of the studies came to the conclusion whether the opioids use is or not a risk factor.

One of the analgesic techniques used currently in ICUs, and which results in improved outcomes, is analgesia-first sedation, which combines analgesic agents first before sedatives.[27] In association, the use of sedatives was pointed by Jeitziner *et al* as a possible risk factor for chronic pain. In this study patients who received higher doses of sedatives had significantly more pain one week after discharge, but not at 6 and 12 months. [24]

Small fiber Neuropathy

Baumbach *et a*l proved patients with small fiber neuropathies had a higher risk of CIRP, reporting higher average pain intensity, pain-related disability, and reduced physical health-related quality of life.[28] From the results of this study it is possible to hypothesize a link between impairment somatosensory function, pain or discomfort and slowed recovery. Therefore screening of somatosensory function in an early phase after ICU discharge could help identify patients at risk of long-term impairments.[28]

Temporal evolution and pain intensity

One of the studies presented determined the incidence of pain after ICU pain at 1 and 6 months.[22] So when the results show a significant improvement between PSEQ scores between 1 and 6 months, we attribute this improvement to the resolution of acute cases, with only some of the pain evolving to chronic pain. 46% of patients reported pain at 1 month which can easily be explained due to the invasive care performed in the ICU. The surprise was that 28% of the patients in the same sample registered pain 6 months after ICU discharge. So, approximately 60% of the patients with acute pain in the recent post discharge developed chronic pain at 6 months. [22]

The majority of the studies included in this review did not allow to establish long term conclusions on the temporal evolution of chronic pain as its prevalence is rarely analysed more than one year after ICU discharge. Cuthbertson *et al* did a 5-year cohort study which allow to have a better idea of the time evolution of pain rather than a screenshot of a particular moment in the patient's recovery after ICU discharge. His study demonstrated a fall in the physical aspects of quality of life at 3 months after ICU discharge, followed by a slowly improvement over the first year, reaching pre-morbid states levels. However, later on, between 2,5 and 5 years after ICU discharge, there was a markedly fall in the physical component scores.[23] In fact, in the population sample the fall in the physical component scores seems to be greater than the general population.[23]

In terms of pain intensity, 49% of the patients reported pain (mild to moderate) 3 months after ICU discharge. In that pain group at 3 months, 52% did not use any pain treatment. However one year after ICU discharge 38% of the patients reported pain and of these only 37% did not use any pain treatment. [19] In Baumbach *et al* study a high percentage of patients with CIRP (45%) reported moderate to severe pain 6 months after discharge.[17] In this study, compared with control data, ICU patients (septic and nonseptic) reported significantly higher levels of average pain and interference scores, both at ICU discharge and at 6 months after compared with controls[17], highlighting the higher intensity of pain in ICU survivors than in the general population.

Impact on the quality of life

Recent studies showed that patients with chronic intensive care related pain (CIRP), reported significantly lower health-related quality of life than ICU patients without CIRP.[16] Cuthbertson *et al*, showed that at least 75% of the physical component scores in the quality of life assessment tool, were below the population mean during the 5 years after ICU discharge[23], showing its perpetuation in time.

Timmers *et al* study reported that 6 or more years after ICU discharge, ICU survivors still experience considerable difficulties in their health-related quality of life.[9] In the same line, Jagodic *et al*, in a

study comparing the outcome and quality of life in septic or trauma patients admitted to the ICU, reported that almost 60% of the patients had problems with daily activities 2 years after discharge and 56% had mobility difficulties. [3] These results raised the question whether the impact on patient's quality of life was due to pain/physical impairment or cognitive disability. A study from Hayhurst and collegues in 2018 demonstrated that pain alone had an interference in patients daily activities, meddling with their ability to work, sleep, participate in normal daily activities and enjoy life. [20] Between 6 and 12 months after ICU discharge about 1/3 of the survivors of critical illness reported CIRP, which is associated health related quality of life disability.[16] Also, Baumbach *et al*, reported that 60% of the CIRP patients had moderate to severe pain interference in daily life, family activities and work.[17]

In Battle *et al* study 32% of patients with persistent pain 6 months after ICU discharge sought the help of a healthcare professional for pain management.[15]

Jagodic *et al*, stated that survival and quality of life after critical care are independent variables.[3]

Limitations

This literature review has some limitations. Firstly, chronic pain was assessed in different timelines over the different studies, making comparisons challenging. Also, the different tools used to assess pain may explain some of the differences in the results. Moreover, most studies did not used specific tools validated for pain assessment. Another limitation is that there is no widely accepted definition of chronic pain after ICU discharge, so various definitions were used in the several studies. An important aspect is none of the studies defined the type of pain (for example nociceptive, neuropathic or visceral). Lastly, the role of transition from acute to chronic pain and pain management techniques in the development of chronic pain should have been further investigated. In fact, the majority of the studies did not evaluate the possibility of the pain relief strategies used in the ICU having an impact in chronic pain.

Likewise limitations were also found in the different studies. The assessment of the baseline data was, in the majority of the studies done, retrospectively leading to limited data and possible recall bias. This was particularly relevant in the assessment of chronic pain pre-ICU admission. Several studies also had a low response rate which may have introduced a nonresponse bias. In other words, due to the low response rate, it is possible that patients with pain were more prompt to answer the questionnaires and participate in the study than patients without pain. Furthermore, there were only a few studies in which patient's admission diagnosis was taken into consideration. In none of the studies pain aetiology was assessed.

Conclusions and Recommendations

Chronic pain is a condition much more prevalent in ICU survivors than one could think, with prevalence and incidence at 6 months after ICU discharge ranging from 22 to 44%. In fact, the major problem with post ICU chronic pain is health related quality of life impairment and pain is one of the main reasons for this outcome.

Patients with chronic intensive care-related pain do not only report high pain intensities but also report a high burden of pain. Indeed, 60% of the CIRP patients reported having moderate to severe interference of pain in daily life, family activities and works.[17] These results reveal the need for an earlier and better pain management.

In the various studies analysed, several risk factors for chronic pain were mentioned, such as sepsis, age, severity of illness (associated with longer mechanical ventilation and hospital length of stay), pre-existing chronic pain and small fibers neuropathy. Still there is a need for further investigation of each one to confirm its interference in the development of chronic pain and determine possible areas of preventive action.

Patients with chronic intensive care-related pain reported significantly lower health quality of life than patients without chronic pain. Even 5 years after ICU discharge, at least 75% of the physical component scores in the quality of life assessment tool were below the population mean.[23]

The need for further investigation in this subject is evident. A multicentre prospective study with standardized timeline and assessment tools of pain would shed a new light to a still developing but important subject.

Key messages

- Chronic pain in ICU survivors is highly prevalent (at 6 months ranging from 22 to 44%)
- Various risk factors have been presented such as sepsis, age, severity of illness, pre-existing chronic pain and small fiber deficits, but needing further investigation
- The most common pain site is the shoulder, and there is no significant relation between the localization of pain and admission diagnosis.
- 45% patients with CIRP report moderate to severe pain 6 months after discharge
- Patients with chronic intensive care-related pain reported significantly lower health quality of life than patients without chronic pain.

Annexes

Table I – Summary of articles

Title/Author	Number of patients	Type of ICU	Data collection	Questionaire applied	Moment of evaluation
Batle, *et al*. – Chronic pain in survivors of critical illness: a retrospective analysis of incidence and risk factors[15]	196 patients	General ICU (medical and surgical) in a teaching hospital in the south of wales (Morriston Hospital)	September 2011 to February 2012	BPI	In the period between 6 months to 1 year after ICU discharge
Langerud, *et al*. – Prevalence, Location and characteristics of chronic pain in intensive care survivors [19]	118 patients	Two mixed ICUs (medical and surgical) in a Olso University Hospital, a tertiary referral hospital	May 2010 to January 2014	BPI	3 months and 1 year
Baumbach, *et al*.- Chronic intensive care-related pain: exploratory analysis on predictors and influence on health-related quality of life [16]	204 patients	Mixed ICUs of Jena University Hospital	September 2011 – December 2014	German Pain Questionnaire	6 and 12 months
Baumbach *et al*. – Prevalence and characteristics of chronic intensive care-related pain: the role of severe sepsis and septic shock [17]	207 septic and nonspetic survivors of critical care and 50 healthy controls	Mixed ICUs of Jena University Hospital	September 2009 – December 2014	German pain questionnaire	6 months
Baumbach, *et al*. – Somatosensory functions in survivors of critical care [28]	84 critical illness survivors and 44 controls	Medical and surgical mixed ICUs -Jena University Hospital	September 2011- December 2014	German Pain Questionnaire and SF-36	6 months
Boyle, *et al*. – The effect of chronic pain on the quality of life amongst intensive care survivors [22]	99 patients	General ICU of a multidisciplinary tertiary hospital (Prince of Wales Hospital)	2 September 2001 to 20 May 2002	Pain scale and self-efficacy questionnaire (PSEQ) and SF-36	1 and 6 months
Hayhurst *et al*. – Pain and its long time interference of daily life after critical illness [20]	295 patients	Medical and surgical ICU Vanderbilt University Medical Center and Saint Thomas	2006	BPI	3 and 12 months

		Hospital Nashvillle, TN			
Cuthbertson *et al*. – Quality of life in the five years after intensive care: a cohort study [23]	300 patients	General ICU in a Scottish tertiary teaching hospital	May 2001 – April 2002	SF-36	3, 6 and 12 months and 2,5 and 5 years
Timmers, *et. al* – Long-term Quality of Life after surgical intensive care admission [9]	834 patients	Surgical ICU of a Dutch teaching hospital	January 1995-February 2000	EuroQoL-6D	Patients were contacted in February 2006
Jeitziner *et al*. – Long-term consequences of pain, anxiety and agitation for critically ill older patients after an intensive care unit stay [24]	145 older patients (ICU group) and 146 comparison group (age-matched participants from the community)	Medical-surgical ICU in a university hospital Switzerland	December 2008-April 2011	Numeric rating scale (0-10)	1 week, 6 and 12 months
Granja, *et. al* – Quality of Life of survivors from severe sepsis and septic shock may be similar to that of others who survive critical illness [21]	184 patients admitted to the ICU with severe sepsis or septic shock and 295 patients admitted to the ICU without sepsis (control group)	Medical and surgical ICU of a tertiary care hospital	March 1997-March 2001	EQ-5D (EuroQol five-dimensions)	6 months
Jagodic, *et al*. – Long term and quality of life of patients treated in surgical intensive care: a comparison between sepsis and trauma [3]	164 patients (98 trauma patients and 66 patients with sepsis)	Surgical ICU in a teaching general hospital	January 2003 – December 2003	EuroQoL-5D	2 years

Table II – Studies results – incidence or prevalence of pain

Study		Incidence or prevalence of pain (%) and moment of evaluation							
		1 month	3 months	6 months	12 months	2 years	2,5 years	5 years	6-11 years
Battle *et al*.[15]	P			44					
Langerud *et al*.[19]	I		49		38				
Baumbach *et al*[16]	P			33	29				
Baumbach *et al*[17]	P			33,2					
Boyle *et al*[22]	I	46		28					
Hayhurst *et al*[20]	P		77		74				
Cuthbertson *et al*[23]	I		31	36	48		56	62	
Timmers *et al*[9]	P								57
Jeitziner *et al*[24]	I			22	15				
Granja *et al*[21]	I			29					
Jagodic *et al*[3]	I					56			

Caption: P- prevalence of pain; I- incidence of pain

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