Surgical Oncology: Evolution of Postoperative Fatigue and Factors Related to Its Severity

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Background: Fatigue has been reported by many patients undergoing surgery and is associated with a negative prognosis. The factors associated with postoperative fatigue and its evolution during the postoperative period are unclear. Adequate fatigue measurement instruments are necessary to obtain reliable evaluations and to direct effective care to control fatigue in this patient population.

Objectives: This article describes the evolution of postoperative fatigue in patients with

cancer as well as related factors.

Methods: A review of the literature using the CINAHL® and PubMed databases was undertaken.

Findings: The prevalence of moderate and severe fatigue varies during the postoperative period, with a reduction in the 12 months after surgery. Various factors (e.g., stress, anxiety, depression, pain, changes in sleep patterns) seem to influence the severity of fatigue. More evidence is needed to explore the relationship between immediate postoperative fatigue and the evolution of fatigue during the period following surgical treatment for cancer.

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urgery is considered to be one of the most important treatments in oncology, despite advances in other treatment modalities. In fact, surgical interventions account for the largest number of cures after a cancer diagnosis (Rosenberg, 2011). More than 60% of patients with cancer undergo surgical intervention, which has indications for prevention, diagnosis, disease staging, cure, and palliation of symptoms (Gillespie, 2011; Rosenberg, 2011). Surgery can be used as the sole treatment strategy or in combination with radiation therapy and/or chemotherapy (Varricchio, 2004).

Even when surgical procedures have positive outcomes, they may also be accompanied by unpleasant side effects. In the perioperative period, fatigue is one of the most common side effects and is acknowledged by many patients as the primary side effect (Paddison et al., 2009). Fatigue is defined as an oppressive feeling with sustained exhaustion and decreased ability to perform physical and mental work at usual levels (Herdman, 2012). Fatigue is characterized by feelings of tiredness, lack of

energy, inability to maintain a usual routine, impaired libido, and verbalization of a constant lack of energy (Herdman, 2012).

Since the 1970s, researchers have been intrigued by the observation that some patients felt more tiredness and had more difficulty returning to normal activities following a surgical procedure than others and began investigating the recovery process (Schroeder & Hill, 1993). In addition, surgeons began to pay attention to tiredness following surgery, labeling it "postoperative fatigue." They also noticed that this fatigue was related to a series of physiologic changes caused by surgical trauma, as well as to the duration of the operation (Christensen, Hougård, & Kehlet, 1985; Christensen & Kehlet, 1993; Rose & King, 1978).

Several studies have pointed to fatigue as a common symptom in the postoperative period (Paddison et al., 2009; Rubin, Hardy & Hotopf, 2004). However, although type of surgery seems to be the main predictor of postoperative fatigue (Paddison et al., 2009; Rubin et al., 2004), how it evolves during the postoperative period remains unclear, as does whether the factors associated with fatigue in patients undergoing surgery are the same as those

experienced by patients undergoing ambulatory antineoplastic treatment. In addition, the adequacy of measurement instruments used to measure fatigue in patients undergoing surgery is unknown.

Many patients with cancer experience fatigue after surgery, and several psychosocial factors are associated with its presence. Using the CINAHL® and PubMed databases, a literature review was conducted to explore fatigue during the postoperative period and identify tools to measure postoperative fatigue. No restrictions were imposed on publication date, and articles written in English, Portuguese, and Spanish were included. The combined key words and medical subject heading terms (MeSH) used were fatigue OR tiredness OR exhaustion AND post-operatory OR postoperative OR perioperatory OR surgery OR surgical AND cancer OR oncology.

Background

Fatigue is frequently experienced by patients with cancer in all phases of the disease (Trudel-Fitzgerald, Savard, & Ivers, 2013). It can be the first sign, starting prior to treatment and progressively worsening. Depending on the population studied and the method of evaluation, the prevalence of fatigue is as much as 99% (Ergun, Eyigor, Karaca, Kisim, & Uslu, 2013). After surgery, postoperative fatigue arises as a feeling of unpleasantness and distress that is influenced by subjective and behavioral symptoms. These feelings may make patients reluctant to mobilize in the postoperative period (DeCherney, Bachmann, Isaacson, & Gall, 2002; Rose & King, 1978). Fatigue is reported by patients even in situations in which no postoperative complications exist (Christensen, Bendix, & Kehlet, 1982).

Surgeons and researchers have observed that fatigue is broader than physical tiredness and is closely related to the emotional state of the patient (Salmon & Hall, 2001). For example, patient expectations regarding postoperative results, in addition to anxiety and depression, have been reported as factors that may affect levels of postoperative fatigue (Wagener & Windsor, 2003). The exact triggering mechanism of fatigue is unclear; however, various mechanisms and interrelated physiologic (e.g., anemia, poor physical condition, cancer), psychological (e.g., anxiety, depression, stress), situational (e.g., negative events in life), and environmental (e.g., noise, light) factors may prompt the occurrence of fatigue (Alibhai et al., 2007; Herdman, 2012; Ream & Richardson, 1996).

Assessment of Postoperative Fatigue

The assessment of fatigue is complex because it is a subjective, multifactorial, and multidimensional symptom (Mota & Pimenta, 2007). In addition, selection of an instrument to measure fatigue is influenced by the perspective of the clinician regarding fatigue and also by the different theoretical frameworks of each instrument. Several instruments have been used for the assessment of postoperative fatigue.

The instruments used to assess postoperative fatigue are essentially the same as for assessment of fatigue in patients receiving outpatient treatments, such as chemotherapy, radiation therapy, or hormone therapy. Most instruments have not been tested for

validity and reliability in patients undergoing surgery, raising doubt about the precision of the results obtained. The most used instrument is the Visual Analog Scale (VAS). The VAS is a one-item scale, 100 mm long, with scores ranging from 0 (no fatigue) to 100 (worst fatigue you can imagine) in which patients point to or mark on the line how fatigued they feel at a particular moment. Although the VAS is a unidimensional tool, limiting the full understanding of fatigue's physical and mental components (Lin, Chen, Yang, & Zhou, 2013), it is strongly recommended as a screening tool; if a patient scores higher than 40 mm, a multidimensional instrument should be applied.

The Identity-Consequence Fatigue Scale (ICFS) is the only instrument available, to date, that has been designed and validated specifically for the evaluation of postoperative fatigue (Paddison, Booth, Hill, & Cameron, 2006). Although the ICFS has proved valid for the assessment of fatigue in patients in the postoperative period, it did not establish a cutoff point that could direct its clinical applicability in the diagnosis, quantification, and characterization of fatigue in surgical care units. Its internal consistency, measured by the Cronbach alpha, is greater than 0.85 in all components, which indicates it to be a reliable tool.

Selecting a fatigue assessment tool may be challenging because more than 30 measurement instruments are available in various forms (e.g., questionnaire, test, scale) (Mota & Pimenta, 2007). In regard to building knowledge, the large amount of instruments hampers the comparison of results obtained from different studies. For this reason, the current authors suggest the use of a standard, simple, reliable, and valid tool to systematically assess fatigue, which will allow the monitoring of this symptom and provide effective control of fatigue in patients undergoing surgery.

Evolution of Fatigue in Patients Undergoing Surgery

Possible predictors of the severity of fatigue during the postoperative period are major surgery, surgery to treat relapses, and the experience of a second surgical procedure for the same diagnosis (Christensen & Kehlet, 1993; Rubin et al., 2004). Patients who present with higher fatigue in the preoperative period will be more likely to develop severe fatigue in the immediate postoperative period (Rotonda, Guillemin, Bonnetain, Velten, & Conroy, 2013).

Several studies have shown that fatigue severity varies across the trajectory of the pre- and postoperative period. In the preoperative phase, the prevalence of fatigue is about 20% (Tsunoda, Nakao, Tsunoda, Watanabe, & Matsui, 2010) with mild intensity in most cases (Andikyan et al., 2012; Lockefeer & De Vries, 2013; Minig et al., 2013). In patients undergoing chemotherapy or neoadjuvant radiation therapy, the intensity of preoperative fatigue tends to increase and reaches a moderate level (Barbour et al., 2008; Mollberg et al., 2012; Schrepf et al., 2013). This increase is often associated with anxiety, suggesting that anxiety is a modulating factor of the intensity of fatigue in the preoperative period (Okuyama et al., 2000).

Knowledge gaps about the intensity of fatigue in the immediate phase of the postoperative period (i.e., 24 hours following surgery) were found. Only one study showed that a quarter of

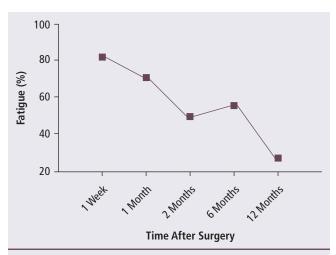


FIGURE 1. Schematic Representation of the Prevalence of Moderate or Intense Fatigue in the Postoperative Period Based on a Review of the Literature

patients had significant fatigue in the immediate postoperative period (Goldstein et al., 2012). In fact, most of the evidence related to the postoperative period was obtained during the first seven days after surgery (see Figure 1).

The severity of fatigue after the first seven days was moderate to intense for more than 80% of patients (Lin et al., 2013; Rotonda et al., 2013; Schmidt, Daun, Malchow, & Küchler, 2010). Patient performance status, quality of life, pain, sleep, stress, depression, and expectations regarding a curative effect of the surgery are associated with level of fatigue during this time (Huang, Chen, Liang, & Miaskowski, 2014; Lin et al., 2013; Montgomery, Schnur, Erblich, Diefenbach, & Bovbjerg, 2010).

A moderate or intense level of pain remained for about 70% of patients for as long as one month after surgery (Andikyan et al., 2012; Kaltoft, Gögenur, & Rosenberg, 2011; Minig et al., 2013; Mollberg et al., 2012; Taira et al., 2011; Tsunoda et al., 2010). Among patients with moderate to intense fatigue, the intensity was higher for those who started adjuvant treatment (Tsunoda et al., 2010) and had required open surgery instead of laparoscopic approaches (Kaltoft et al., 2011). One month after surgery, some patients experienced partial or complete relief of fatigue, often with situations in which the cancer was not present during analysis of the surgical specimen (Michielsen, Van der Steeg, Roukema, & De Vries, 2007). Although the intensity may be mild, the prevalence of fatigue is still significant one month after surgery, with more than 60% of patients reporting fatigue (Liu, Ercolano, Siefert, & McCorkle, 2010).

The prevalence and intensity of fatigue tends to decline two to four months after surgery. Fagundes et al. (2011) and Liu et al. (2010) found that the prevalence of fatigue varied from 12%–49% of patients, with most experiencing fatigue of a mild intensity (Huang et al., 2014; Prue, Rankin, Cramp, Allen, & Gracey, 2006; Sarna et al., 2008). Schmidt et al. (2005, 2010) found that men had mild fatigue after surgery for rectal cancer, whereas women who had undergone the same surgery reported moderate fatigue. The relationship between gender and fatigue may be associated with the fact that women, in general, present with the most intense sleep disorders and greater sleep impairment, along with worse

physical functioning and overall health status (Schmidt et al., 2005, 2010). In addition, throughout postoperative follow-up treatment, even 12 months after surgery, women experienced significantly higher strain and overall burden (Schmidt et al., 2005, 2010).

Six months after surgery, fatigue often returned to a prevalence similar to that observed at the first month after surgery. In several studies, more than 60% of patients experienced fatigue (Liu et al., 2010), and many experienced moderate to severe fatigue (Den Oudsten, Van Heck, Van der Steeg, Roukema, & De Vries, 2010; Djärv, Lagergren, Blazeby, & Lagergren, 2008; Viklund, Wengström, Rouvelas, Lindblad, & Lagergren, 2006; Wikman, Johar, & Lagergren, 2014). The number of surgical treatments is not a factor in experiencing fatigue (Den Oudsten et al., 2010); instead, baseline, preoperative fatigue, anxiety, depression, and sleep are factors that influence the evolution of fatigue in the postoperative period (De Vries, Van der Steeg, & Roukema, 2009; Sugawara et al., 2005; Van Onselen et al., 2013). Prolonged fatigue and longer recovery time was observed in patients after extensive esophageal tract surgery (Viklund et al., 2006). A cohort study showed a symptom cluster of fatigue, pain, insomnia, and dyspnea in 30% of 402 patients with esophageal cancer who reported symptoms six months after surgery; the median survival time for patients with this cluster was 18 months (Wikman et al., 2014).

Verschuur et al. (2006) found that the prevalence of significant fatigue in patients with esophageal cancer was 56% at 12 months after surgery. In a study by Winters-Stone, Bennett, Nail, and Schwartz (2008), postoperative fatigue was reported by 58% of older adult women with breast cancer who underwent adjuvant treatment, as well as had high body mass index values and lower muscle strength. One year after surgery, the intensity of fatigue varied from mild (60%) to moderate (30%) (Den Oudsten et al., 2010; Hubbard, Gray, Ayansina, Evans, & Kyle, 2013; Kim et al., 2012; Lowery et al., 2014). In a study by Lowery et al. (2014), fatigue was found to be related to other symptoms, such as dyspnea and pain. In two studies reporting the prevalence of fatigue longitudinally, fatigue at 24 months and at 36 months after surgery showed significant intensity, ranging from moderate to severe (Djärv et al., 2008; Schmidt et al., 2005; Taira et al., 2011). Factors related to this prolonged fatigue were not reported or discussed. However, based on the current authors' practical experience, the intensity of fatigue rises later in the trajectory because of other factors, such as recurrence, disease progression, or change in treatment protocol.

These findings highlight the oscillatory prevalence and intensity of fatigue during the postoperative period, with a tendency to decrease 24 months after surgery. In addition, although the intensity of fatigue decreased during the postoperative period, it has been reported and observed even 36 months after surgery. Symptom clusters seem to intensify the manifestation of fatigue.

Although some evidence reveals the course of postoperative fatigue in the immediate and late postoperative periods, the findings are only somewhat consistent. A lack of studies exist regarding the immediate postoperative phase, indicating a need for fatigue research to investigate and possibly predict the evolution of fatigue across later stages of recovery following surgery, as well as the intersection of disease-related factors and symptom clusters.

Implications for Practice

- Understand that the incidence and intensity of postoperative fatigue reach their highest points one month after surgery, and then typically decline to preoperative levels.
- Assess and measure fatigue in patients undergoing surgery using valid and reliable tools.
- Be aware that anxiety, expectations about the surgery outcome, and the surgery itself are factors associated with postoperative fatigue.

Conclusion

Fatigue is recognized as a phenomenon that directly affects patients undergoing surgical treatment and requires the attention of healthcare professionals. The assessment and diagnosis of fatigue should be carried out in a systematic and standardized manner, preferably using self-report and multidimensional instruments to capture related symptoms. Preoperatively, the intensity of fatigue tends to be low and its intensity mild. Fatigue is prevalent and severe in patients undergoing surgery during the immediate and late postoperative periods. In the first month after surgery, the incidence and intensity of postoperative fatigue increases significantly. Despite the reduction in intensity two months after surgery and onward, fatigue remains present even one year after surgery. The fact that many patients still report fatigue for as long as 36 months after surgery makes necessary the identifying and managing of fatigue in the early stages of the postoperative period, with the expectation of reducing its prevalence in the long term. Factors associated with postoperative fatigue, such as pain, sleep issues, and emotional factors (e.g., stress, depression, anxiety), must be identified so that interventions can be implemented to prevent and control the fatigue of patients with cancer undergoing surgery.

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