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Optimization of the Treatment Flow of Neurosurgical Patients with a Glioblastoma using the Enhanced Recovery After Surgery Methodology: A Literature Review

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ABSTRACT

Purpose: This study aims to create an elaborated version of the Enhanced Recovery After Surgery methodology, specifically applied to neurosurgical patients with a glioblastoma.

Introduction: Being diagnosed with a glioblastoma is a terminal diagnosis with a median survival rate of 14,6 months. The introduction of an Enhanced Recovery After Surgery can provide a solution for current challenges such as the under-pressure health care system because of a lack of nurses and well-trained nurses in neurosurgical problems. Enhanced Recovery After Surgery benefits the patient, healthcare teams and society.

Methods: A literature review with two different search strategies was conducted. First, the needs and expectations of patients with a glioblastoma were identified. Seventy-five papers from four databases, PubMed, Embase, CINAHL and Cochrane Library, were eligible. Fourteen papers were included in this study. Second, the existing Enhanced Recovery After Surgery protocols were examined. A total of 3,521 papers were screened by two independent researchers, of which 82 met the inclusion criteria and 50 were determined relevant for this study. In this way, an elaborated version of the Enhanced Recovery After Surgery methodology based on the needs of patients with a glioblastoma is created.

Results: Patients with a glioblastoma may face numerous needs. Due to a poor diagnosis and uncertain future, they could feel distressed and anxious. Patients expect more information, support and availability from health professionals. Therefore, it is important for healthcare professionals to make sure that patients do not lose all hope after the diagnosis because losing hope is associated with depression and a poorer quality of life. All these needs were integrated in the Enhanced Recovery After Surgery protocol and combined with new insights from the literature. The first bundle of recommendations in the Enhanced Recovery After Surgery for patients with a glioblastoma belongs to the preoperative phase and includes: information and education, prehabilitation, nutrition support and fasting time, alcohol and smoking, comorbidities and medication. The intraoperative phase includes advice about antibiotics, body temperature, craniotomy, stitches and extubating. Finally, the postoperative phase includes recommendations regarding thromboembolism, nausea and vomiting, analgesics, oral nutrition, fluids, invasive lines, mobilization, urinary catheter, drains, discharge, telephone follow-up and social and emotional support.

Conclusion: The established protocol needs to be constantly adapted to new evidence. Only with an appropriate multidisciplinary collaboration and thoughtful introduction of the Enhanced Recovery After Surgery, the implementation and sustainability of the new Enhanced Recovery After Surgery protocol will succeed in daily practice.

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Introduction

Being diagnosed with a glioblastoma is a terminal diagnosis with a median survival rate of 14,6 months [1,2]. In Belgium, 764 persons are diagnosed with a glioma in 2020 of which 564 persons were diagnosed with a glioblastoma [3]. According to approximately 11,5 million inhabitants in Belgium, 4,9 per 100,000 persons are diagnosed with a glioblastoma in 2020 [4]. The classification of gliomas is based on the grading system of the World Health Organization and indicates that grade one is the least aggressive form and grade four, which includes the glioblastoma, is the most aggressive form [5]. Due to the severity of the diagnosis and the majority of glioblastoma patients, was chosen to focus on patients with a glioblastoma.

Moreover, intracranial brain tumors belong to one of the most important care programs of the neurosurgical department of the

University Hospitals Leuven, Belgium [6]. Although the survival time is low, these patients need to receive the best possible quality of life. At the moment, the health care system is under pressure because of a lack of nurses and additional a lack of well-trained nurses in neurosurgical problems. The introduction of an Enhanced Recovery After Surgery (ERAS) can provide a solution to these problems.
ERAS has a history that goes back to 1997 [7]. At that moment, Professor Kehlet of Denmark first described fast-track surgery [8]. This approach was pioneered in colorectal surgery and since then has spread to other surgical fields [9]. In 2001, a study group of academic surgeons in London started the concept of ERAS which puts more emphasis on the improvement of postoperative procedures rather than only the shortening of hospital stays [10,11]. The concept of ERAS is an evidence-based standardized framework for a specific pathology, rather than an individually adapted plan [12,13]. Rollins et al. make clear that 'An ERAS pathway typically includes approximately 20 interventions (elements or components) divided into three distinct phases – the preoperative, intraoperative and postoperative periods' (2021).

Since the concept of ERAS was introduced, there has been a shift to reduced hospital length of stay and improved postoperative quality of life, without higher re-admission rates [14,15]. Furthermore, randomized controlled trials (RCTs) and meta-analyses have shown that ERAS reduces global postoperative morbidity by 50% [16]. For healthcare organizations, ERAS is an attractive concept because of patient safety, efficiency, cost-effectiveness and reduction of clinical variance, which is essential in the current economic climate [13]. Therefore, ERAS is a benefit for the patient, healthcare teams and society. The patient becomes an actor in his own care and his participation is the reflection of the success of the ERAS [15]. The goal of ERAS is to regain the same physical and psychological state the patient had before surgery and this by reducing stress and the inflammatory response triggered by the surgery [17]. In conclusion, ERAS is an effective and valuable tool for improving patient outcomes and an improved recovery after surgery [18]. In recent years, the safety and effectiveness of ERAS has been widely recognized by the medical community [19].

In neurosurgery, the first ERAS program started in spinal surgery in 2017 [20]. In 2018, the first ERAS protocol for elective craniotomy has been reported (Wang et al., 2018). A first review with an overview of ERAS recommendations for craniotomy in patients with a brain tumor was written in 2022 [21]. Despite this, in neurosurgery there are no evolving adaptions of the concept of ERAS comparable to other surgical fields [22]. A single-center RCT concluded that an ERAS program in glioma patients is widely supported and the aim is to improve health-related quality of life [23]. Neurosurgeons positively welcomed ERAS and observed a decrease in intensive care unit (ICU) admissions, a decreased length of stay, decreased patients costs, lower readmission rates and increased patient satisfaction [22].

This review of the literature is value-added because it is one of the first Enhanced Recovery After Surgery methodologies for patients with a glioblastoma that is composed in theory. This protocol is valuable because it gives an impetus to introduce an Enhanced Recovery After Surgery protocol with concrete recommendations that are relatively simple to implement. In addition, it can be said that this protocol is innovative because it combines the needs of the patient with a glioblastoma with the elements of the Enhanced Recovery After Surgery. In this way, the patient can be fully placed at the center of his treatment and be provided by the best possible care.

Methods

This study attempts to answer the following research question by applying a literature review: 'What does optimization of the treatment flow of neurosurgical patients with a glioblastoma look like using the ERAS methodology?'.

More specifically, a literature study is conducted with two different search strategies. On the one hand, the needs and expectations of neurosurgical patients with a glioblastoma are mapped out. On the other hand, the existing ERAS pathways are examined. In this way, an elaborated version of the Enhanced Recovery After Surgery methodology, specifically applied to the needs of neurosurgical patients with a glioblastoma is created.

Before an ERAS for patients with a glioblastoma could be made, the needs of these patients must be discovered. With this information, a broader view on the disease and its treatment can be obtained. In this way, a patient-centered ERAS specifically for patients with a glioblastoma can be established. The search strategy for the needs of patients with a malignant glioma was used and adapted to four databases: PubMed, Embase, CINAHL and Cochrane Library. A total of 75 papers were found and screened by two independent researchers on title and abstract, nineteen of which were eligible for further screening on full text. Fourteen papers were finally included in this study. Inclusion criteria are patients of eighteen years and older, diagnosed with all grades of glioma, focus on needs of patients and at least three patients participating in the study. Exclusion criteria contain research about caregivers, patients less than eighteen years old, other neurosurgical tumors, no focus on needs of patients and literature before 2010. Despite the indispensable role of caregivers in the life of the patient, the needs of caregivers were kept out of perception in this study.

A second search focused on the existing ERAS pathways. This will make the concept of ERAS and its most necessary elements clear. It will create a view that is as broad as possible to adapt to glioblastoma patients. ERAS since 2010 until now, neuropathology and papers about the structure of ERAS are included. Exclusion criteria contain papers focusing specifically on a pathology outside of neurosurgery and no focus on the content of ERAS. The following search strategy was used in Pubmed: ((((enhanced recovery [Title/Abstract]) AND (surgery [MeSH Terms])) AND (surger*[Title/Abstract])) NOT (child [MeSH Terms])) NOT (child*[Title/Abstract]). In total, 3,521 papers were found and screened on title and abstract by two independent researchers using Rayyan. Differences in the screening process were discussed and resolved. Finally, 82 papers met the inclusion criteria. Eighteen of them had no free access, three were written in German or Chinese, one paper had been retracted and eleven of them contained no relevant information when read full text. Lastly, 50 papers were included in this study of which one was found using the snowball sampling method. Data saturation was obtained and no more databases are used.

This study is conducted in collaboration with the neurosurgical ward of the University Hospitals Leuven.

Results

Needs of Patients with a Glioblastoma

Patients with a glioblastoma may have numerous needs. Due to a poor diagnosis and uncertain future, they may feel distressed and anxious [24]. Patients can feel anxious about diagnosis, discussion of prognosis, anticipation of scan results, point of recurrence and preparation of end-of-life discussion. Moreover, they may feel death anxiety and this expresses in shock, anger, sadness

or fear [25]. A study by Halkett et al. discovered that the level of education of the patient is the best predictor of their distress accordingly the lower the education, the higher the level of distress (2015). Patients may experience distress because of changes in personality, memory loss and communication problems [26]. Renovanz et al. found that when the distress is higher, the needs are also higher [27]. A nurse specialist can fulfill these needs as a contact person for the patient and caregiver and the nurse can build a relationship between the team and patient [25]. Trad et al. mentioned that 'A neuro-oncology-specific care coordinator is well positioned to facilitate symptom and needs assessment, psychological support and referrals or intervention throughout the care continuum' [28]. Professional empathy and emotional support can help the acceptability of the disease [26]. The caregiver has a critical role and needs to be included in the care relationship [29]. It is also easier for the patients if they see the same professional every time [30]. A case study reported fragmented information when it was given by several healthcare professionals and this may cause feelings of uncertainty, loss of control and frustration [31]. In summary, patients expect information, support and availability from professionals [30].

Information needs to be tailored individually and without medical jargon [24,32]. Patients want to have opportunities to receive more postoperative information, information about available resources, the illness, treatment options, their condition and possible lifestyle changes [25,26,33]. They want information from different sources such as written, verbal, how they can get access to other health care professionals [34]. Due to shock, information absorption and retention could be difficult at the beginning of their diagnosis [26]. 40-80% of the information delivered by healthcare providers is instantly forgotten by patients and there is a discrepancy between the perceived and actual understanding of the patient [35]. Combining the shock of having a potentially fatal disease with all the symptoms, could make it difficult to understand and retain information [31]. Frequent contact helps to foster communication [36]. mentioned that 'active exploration of the patient's disease perspective is imperative in understanding and meeting the needs of each patient.' Patients appreciate it to see the scan of their glioblastoma and to have the possibility to ask questions about it [30,31].

Furthermore, patients report loss in different ways: they notice loss of independence, self-loss and loss of relationships [25]. Sometimes they do not feel recognized as a person in their totality and this may bring feelings of humiliation and loneliness. Feelings of depression and restlessness could also have a big impact on them [32]. A glioblastoma may cause changes in physique, seizures, drowsiness, headaches, immobility, short-term memory issues, mood swings, visual or speech disorders, personality changes and decision-making problems [31,37]. Sometimes, patients lose their independence and have decreased skills in communication [33]. Patients can have worries about the financial impact that the disease could have [32]. Roles reversals, worries about the impact on the caregiver and losing the ability to be a parent for their children are additional major concerns for patients that may play a role [37].

Therefore, it is important that patients do not lose all hope after the diagnosis [24]. Unfortunately, the diagnosis of glioblastoma is regarded as incurable but the patient can hope that he is one of the 3 to 5% that survives more than three years [38]. A care provider needs to be honest about the diagnosis but also give a little hope. Further, the healthcare professional should be compassionate because losing hope is associated with depression and a poorer quality of life [36]. Patients can find hope in talking, in local community organizations or support groups and with patients who experienced the same as them [32]. Patients with a malignant glioma may have a great desire to exchange experiences with other patients [24]. Patients can find joy in volunteering and exploring new hobbies, they try to cope by having a positive attitude and planning for the near future [37]. A strong relationship with family and children can gives meaning and strength to their life [32].

Enhanced Recovery after Surgery

Preoperative

The first bundle of recommendations from existing ERAS pathways belongs to the preoperative phase. More specifically, ERAS is most successful when the patient is educated about the protocol and if expectations are fulfilled [39]. Patients need to be informed about a number of aspects, such as the surgical pathway, what they can do to prepare before surgery, the optimization of the health condition, what they can expect after surgery and discharge planning [40]. A better understanding and expectation of patient's recovery resulted in improved healthcare according to a systematic review [14].

Furthermore, recovery is not a passive process and already starts preoperatively. To build up a physiological reserve that supports a good recovery, the patient needs to prehabilitate which means he needs to do exercises and have a good nutritional intake before surgery [41]. Exercises such as cardiopulmonary conditioning and muscle strengthening can reduce frailty [14]. Progressive exercises need to be done two to four weeks before surgery because training before surgery is associated with improved outcomes [42,43]. Due to the relative urgent character of the surgery, a period of two to four weeks may not be feasible. Prehabilitation is a process to improve the patient's overall health and to reduce the incidence and severity of current and future impairments [44]. Shanahan and Leissner make clear that 'Surgery can act as a motivational goal to promote healthy behavior change' [45]. Every patient needs to be stimulated to increase their physical activity even if they have limited mobility [12]. However, this is especially true for frail, cognitively impaired or elderly persons, to improve their functional level [44].

Additionally, patients who have a higher risk of malnutrition such as the elderly, chronically ill people and people with active alcohol abuse should be provided with nutritional support in the form of oral nutritional supplements [46]. The guidelines of the European Society for Clinical Nutrition and Metabolism recommend enteral nutrition support for seven to fourteen days before major surgery. Patients with severe malnutrition or who are unable to eat orally are recommended to have seven to ten days of parenteral nutrition [11]. Research has shown that nutrition supplements can reduce the length of stay and infective complications [45]. Furthermore, fasting time before surgery is set at eight hours for solid food, six hours for nonclear liquids and two hours for clear liquids [47]. Contrary to general expectations, these relatively short time periods will not increase the risk of vomiting or aspiration due to anesthesia [48].

Moreover, in general it is recommended to quit alcohol and smoking at least one month before surgery [49]. This may not be feasible due to the urgency of the surgery, but it is recommended to stop alcohol and smoking immediately. This is because excessive alcohol consumption can lead to immune dysfunction, subclinical cardiac insufficiency, arrhythmias and an increased bleeding time. In turn, smoking can increase pulmonary and cardiovascular complications and wound-healing problems [45].

Lastly, comorbidities such as diabetes or hypertension must be kept under control [50]. Acute hyperglycemia is known to cause a pro-inflammatory state and decreased immune system. Therefore, diabetics should be checked and given insulin when necessary. However, normoglycemia is not the goal since stress hyperglycemia is protective in normal amounts [45]. Further, sedatives, hypnotics and opioids prolong recovery because of the inability to drink or mobilize after surgery [51].

Intraoperative

This study includes some advice for the intraoperative phase. First of all, antibiotics should not be given more than 60 minutes before incision. More specifically, the recommendation is a single administration of two grams of intravenous (IV) cefazolin at induction or three grams if the patient weighs more than 120 kg. If the patient has a beta-lactam allergy, clindamycin (600-900 mg) or vancomycin (15-20 mg/kg) should be used. An additional dose should be given intraoperatively if the surgery takes more than four hours or if the patient loses over 1500 mL of blood. In general, prophylaxis is preferred due to its safety, tolerability, cost-effectiveness and antimicrobial efficacy [21]. Furthermore, it is crucial that the patient maintains a core body temperature of 36-37 degrees Celsius in the pre- and intraoperative phase as normothermia can reduce infections, bleedings and cardiac complications [21,52].

In addition, minimalizing invasive craniotomy has benefited a large number of patients who reported a better recovery and an increased level of satisfaction [47]. Incision of dura, muscle and subcutaneous tissue can be closed with interrupted absorbable sutures. Skin incision can be closed with intradermal running suture. These measurements are associated with a shorter length of stay, cosmetic advantages and reduced discomfort [42]. Moreover, the patient is preferably extubated in the operating room and directly transferred to ICU [53]. This might benefit the patient by earlier detection of alternations in conscious levels, which in this case may lead to a faster treatment [54].

Postoperative

This study identifies a collection of recommendations for the postoperative phase. Especially for gliomas, there is an increased risk of venous thromboembolism. Simultaneously, anticoagulants raise the probability of an intracranial hemorrhage. The Neurocritical Care Society and the Society of Critical Care Medicine endorse intermittent pneumatic compression plus low molecular weight heparin (LMWH) or unfractionated heparin (UFH) within 24 hours after craniotomy for malignant glioma patients [21]. The latest systematic review concluded that venous thromboembolism is effective and safe in elective craniotomy and without increased bleeding events [42].

Additionally, routine use of serotonin receptor antagonists and dexamethasone is highly recommended when patients have postoperatively nausea or vomiting [49]. Further, the use of analgesics such as tramadol, gabapentin, pregabalin and nonsteroidal anti-inflammatory drugs (NSAIDs) should be discouraged and non-opioids should be used instead [55]. Evidence has shown that opiates are less effective for craniotomy patients [56]. Furthermore, intramuscular analgesia should be avoided due to the inconsistent absorption and variable efficacy [57].

Moreover, early postoperative oral nutrition has been shown to be safe and well-tolerated [14]. Chewing gum can help to stimulate motility after surgery and is a low-cost and low-risk adjuvant [21,58]. If possible, begin with clear liquids four hours after extubation [21]. Eight hours after surgery, the patient can start with a light diet and nutritional drink [42]. It is recommended to start with a regular diet within 12 to 24 hours [21].

There often occurs inappropriate use of IV fluid pre-, intra- and postoperatively, which results in fluid overload and an electrolyte imbalance [13]. Therefore, once the patient is fully awake, the IV fluid should be removed [43]. If possible, invasive lines and catheters need to be removed within six hours after surgery because this facilitates early mobilization and can decrease the risk of bloodborne infections [21].

Early postoperative mobilization has numerous benefits such as a decreased risk of postoperative complications, increased patient satisfaction and a reduced length of stay. Limb exercises in bed can be done within six hours after waking up from anesthesia [42]. Patients should ambulate 24 hours after surgery and eat out of bed for all meals [43,59]. Generally, early mobilization predicts a good recovery [43].

Furthermore, urinary catheters should be removed within 24 hours to avoid urinary tract infections [21]. A review of glioma patients showed that in 74%, the urinary catheter could be removed within six hours [47]. In addition, surgical site drainage needs to be avoided. In case if drains were placed, remove them as early as possible and within 24 to 48 hours. This measurement is safe and can reduce postoperative discomfort and promote early mobilization [42].

A worldwide trend in neurosurgical care is keeping the patient four to six days in hospital [53]. However, research has shown that earlier discharge after neurosurgery is not only feasible, but also safe, cost-effective and does not increase morbidity rate [23]. That said, the patient needs to meet all the predetermined discharge criteria, which include full consciousness and alertness, adequate pain control with oral analgesics, body temperature in the normal range, ability to eat without aspiration risk, move independently, major laboratory tests within normal limits, head CT scan ruling out early surgical complications and a safe discharge destination [42,53,59]. If discharge criteria are not fulfilled, it is recommended to re-evaluate in 24 hours. A cohort study by Neville et al. showed a reduction in hospital days from five to three days by discharging patients when they met all the discharge criteria [53]. Furthermore, a systematic review found that telehealth improves communication [21]. Therefore, in some ERAS programs, telephone follow-up is available for 24 hours after discharge [50]. An ERAS program after elective craniotomy described telephone follow-ups one, three and six months after discharge [59]. Because of all these measurements, a randomized controlled study observed a higher patient satisfaction in the ERAS group than in the control group [60].

Implementation

In order to successfully implement an ERAS protocol, healthcare workers must understand the benefits of change [61]. Implementation requires teamwork, multidisciplinary collaboration and education for staff and patients [13,62,63]. Continuous measurements and improvements of the elements of ERAS are essential [48]. An ERAS coordinator improves patient education and allegiance to the protocol because compliance with ERAS is a major issue [64,65]. An ERAS coordinator is commonly a nurse who has an important and visible role in ERAS [66,67]. Nurses experience the largest impact of ERAS on their daily

work and notice that some patients do not fit the ERAS pathway because they are too frail or unwell [63]. A retrospective cohort study observed a significant inverse linear correlation between nursing workload and compliance with the ERAS protocol (ρ=-0,42 and P<0,001) [68].

Barriers to implement ERAS are resistance to change, a lack of support from the management, high staff turnover, poor documentation and shortness of time [63]. Moreover, it seems to be easier for large communities and academic settings to implement an ERAS protocol [69]. Schmidt reported that 'the design and implementation of an ERAS protocol must be specific to each hospital and requires input and action from key stakeholders' [48]. At a bare minimum, a convinced surgeon is needed, as well as a nurse, an anesthetist and managerial support to introduce an ERAS program. To look back at the successes and failures of an ERAS program, regular audits must be planned to achieve a sustainable pathway [70].

Discussion

Reflection on Results/Strengths

This research is based on fourteen papers about the needs of patients with a malignant glioma and 50 papers concerning existing ERAS. These papers were combined to answer the following research question: 'What does optimization of the treatment flow of neurosurgical patients with a glioblastoma look like using the ERAS methodology?' Table 1 provides a brief overview of the key findings of the reported results. It represents the first ERAS that meets the needs of glioblastoma patients by combining insights from different sources. The added value of this study is the clear description of the protocol as well as the brief summary accessible to the general public. Previously, research had been conducted about ERAS for glioma patients, but a clearly detailed protocol was lacking. The ERAS protocol contains 22 elements divided into three phases, as previously revealed. The established ERAS is made for general use and could be adapted to the experiences and daily practices of the hospital. It gives building blocks for an elaborated ERAS protocol in the neurosurgical ward. It can be argued that it is extremely important to motivate people to work together on the introduction of ERAS because a person can never succeed alone. A motivated nurse specialist with a focus on neurosurgery can be a good first step.

Limitations

This research has some limitations. During the study of the needs of patients with a malignant glioma, we only focused on the needs of the patients themselves. The needs of caregivers were kept out of perception, but these people obviously play an indispensable role in the life of the patient. Due to limited research on patients with a malignant glioma, studies from 2010 until now were included. As a result, in some perspectives, this study may contain outdated insights.

Furthermore, the search strategy of the existing ERAS was only done in PubMed. Because of this choice, potentially relevant information may have been lost. A restriction of the study is that only papers in English were selected. Additionally, some papers were not available for free in full text. In this way, possibly important results may have been overlooked. Moreover, the protocol is made for adults with glioblastoma, children were not included in the search strategy.

A limited time of one year for this research prevented further thorough analysis of the topic. Moreover, the element of carbohydrate loading is not included in this ERAS despite its general use in some other ERAS programs. Due to changing evidence, it was chosen to not include this subject in the ERAS. Further research could be done to investigate the usefulness of this item. More items can be added to the protocol according to additional evidence.

Implications for further Research

Further studies are needed to implement the role of caregivers in the ERAS protocol. Moreover, further research is needed to evaluate the effectiveness of the protocol. New evidence needs to be constantly integrated since the ERAS is an evolving protocol. The neurosurgical ward of the University Hospitals Leuven wants to integrate an ERAS protocol into their daily care for glioblastoma patients, which was the initiation of this research. However, before the protocol can be integrated, further research needs to be done to implement and sustain the theory in daily practice.

Table 1: Overview of ERAS Protocol

	Item	ERAS protocol
Preoperative	Information and education	✓ Inform about available resources, the illness, treatment options, their condition, possible lifestyle changes and financial costs ✓ Explain the ERAS: how to prepare before surgery, expectations after surgery and discharge planning ✓ Information is tailored individually and without medical jargon ✓ Provide information from different sources: written, verbal and how to get access to other professionals ✓ Provide the opportunity to ask questions and to show the scan of their glioblastoma ✓ Frequent contact fosters communication: nurse specialist as contact person for patient and caregiver ✓ Explore the patient's disease perspective and corresponding needs ✓ Keep in mind that the patient may experience distress because of changes in personality, memory loss and communication problems ✓ Show professional empathy and emotional support ✓ Be honest and compassionate, balance between reality and hope, recognize the patient in his totality
	Prehabilitation	✓ Cardiopulmonary conditioning and muscle strengthening ✓ Progressive exercises 2 to 4 weeks before surgery, this may not be feasible due to the urgent character of the surgery ✓ Important for everybody and especially for frail, cognitively impaired or elderly persons
	Nutrition support and fasting time	✓ Elderly, chronically ill persons and people engaging in active alcohol abuse: 7-14 days enteral nutritional supplements before surgery ✓ Severe malnutrition and people who are unable to eat: 7-10 days parenteral nutrition before surgery ✓ Fasting time: 8 hours for solid food, 6 hours for nonclear liquids and 2 hours for clear liquids
	Alcohol and smoking	✓ Stop both at least one month before surgery, this may not be feasible due to the urgency of the surgery
	Comorbidities and medication	✓ Comorbidities such as diabetes or hypertension must be kept under control ✓ Diabetics should be checked and given insulin when necessary, however within the normal blood sugar range is not the goal ✓ Avoid sedatives, hypnotics and opioids
Intraoperative	Antibiotics	✓ 60 minutes before incision: 2 grams cefazolin IV or 3 grams if patient >120 kg ✓ If beta-lactam allergy: clindamycin (600-900 mg) or vancomycin (15-20 mg/kg) ✓ Additional dose if surgery > 4 hours or patient loses > 1500 mL of blood
	Body temperature	✓ Maintain core body temperature of 36-37 degrees Celsius pre- and intraoperative
	Craniotomy	✓ Minimally invasive craniotomy
	Stitches	✓ Close dura, muscle and subcutaneous tissue with interrupted absorbable sutures ✓ Close skin incision with intradermal running suture
	Extubating	✓ Extubate preferably in the operating room and transfer directly to the ICU
Postoperative	Thromboembolism	✓ Intermittent pneumatic compression plus LMWH or UFH within 24 hours after craniotomy
	Nausea and vomiting	✓ Use routinely a serotonin receptor antagonists and dexamethasone
	Analgesics	✓ Use non-opioids and preferably not intramuscular
	Oral nutrition	✓ Chewing gum can stimulate motility ✓ 4 hours after extubation: start with clear liquids ✓ 8 hours: light diet and nutritional drink ✓ 12-24 hours: regular diet
	Fluids	✓ If patient is fully awake, remove IV fluids
	Invasive lines	✓ Remove within 6 hours after surgery
	Mobilization	✓ 6 hours after anesthesia: limb exercises in bed ✓ Within 24 hours: ambulate + eat out of bed for all meals
	Urinary catheter	✓ Remove within 6 hours ✓ If not possible try within 24 hours
	Drains	✓ Should be avoided ✓ If placed, remove within 24 to 48 hours

	Discharge	✓ When met all the discharge criteria o Full consciousness and alertness o Adequate pain control with oral analgesics o Body temperature within normal range o Ability to eat without aspiration risk o Able to move independently o Major laboratory tests within normal limits o Head CT scan ruling out early surgical complications o Safe discharge destination ✓ Re-evaluate in 24 hours when discharge criteria are not met
	Telephone follow-up	✓ Make telephone follow-up available for 24 hours after discharge ✓ Follow-up after month 1, 3 and 6 after discharge ✓ Preferably done by the same nurse specialist as contact person for patient and caregiver
	Social and emotional support	✓ Exchanging experiences with other patients are desired as well as community organizations and support groups

Conclusion

This study aimed to create an elaborated version of the ERAS methodology, specifically applied to neurosurgical patients with a glioblastoma. Moreover, specific recommendations were done and integrated with the needs of patients with a glioblastoma into the Enhanced Recovery After Surgery. The established protocol needs to be constantly adapted to new evidence. Only with an appropriate multidisciplinary collaboration and thoughtful introduction of ERAS, the implementation and sustainability of the new ERAS protocol will succeed in daily practice.

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Conflict of Interest Statement

There are no conflicts of interest in concerning this research.

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