CASE REPORTS

TAILORED PERIOPERATIVE MEDICINE FOR FRAIL PATIENTS UNDERGOING VASCULAR SURGERY: A NARRATIVE REVIEW

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Abstract

Frailty is a concept that is emerging as an important tool in the preoperative assessment of patients. The incidence of frailty in vascular surgery patients is high and is expected to increase concomitantly with the aging of the population. The identification of these patients and their optimization in the perioperative period can lead to an improvement in their outcomes with a reduction in morbidity and mortality. In this narrative review we address the concept of frailty applied to vascular surgery patients as well as assessment tools for its evaluation. This review focus not only on the most utilized evaluation tools but also on the most recent and specific frailty evaluation instruments that are suitable for vascular surgery patients. Furthermore, we review patient optimization strategies to improve perioperative outcomes.

Keywords: *Frailty, Perioperative Care, Vascular Surgery, Geriatric Anesthesia, Prehabilitation*

INTRODUCTION

Population aging is an expected scenario with consequences for health systems. The increasing number of elderly patients represents a challenge for all healthcare professionals.[1] This is extremely relevant in vascular surgery context due to a strong correlation between the prevalence of vascular disease and increasing age: from 40 to 50 years: 2% and between 51 to 60 years: 3.5%, up to 22.3% and 32.5% after 80 and 90 years old, respectively.[2] Although endovascular surgery is emerging as a safer option for patients considered high risk for open surgery, some elderly patients still suffer from major postoperative complications, loss of quality of life or even death.[3] Albeit chronological age correlates with the burden of cardiovascular disease, evidence indicates that neither chronological age nor the American Society of Anesthesiologists physical status classification system completely correlate with the risk of perioperative and postoperative events.[1]

Frailty is a syndrome marked by diminished physiological reserves, increasing individuals' susceptibility to adverse outcomes due to reduced tolerance for physical, psychological, and psychosocial stressors.[4] Frailty is a better predictor of postoperative morbidity, mortality and adverse functional outcomes than chronological age or comorbidity indexes and therefore it is a more precise way to evaluate vulnerable patients.[5] Likewise, frailty is highly prevalent in vascular surgery patients and its incidence ranges from 20% to 60%.[5]

The main goals of this narrative review were to provide an overview of frailty and its relevance to perioperative clinicians, to highlight the importance of assessing frailty particularly in vascular surgery patients and to discuss interventions for perioperative optimization.

METHODS

This review provides an overview of frailty in vascular surgery. We performed a focused electronic search using the PubMed database. We included English-language original and review articles published between January 2001 and December 2023. The following combinations of MESH terms were used: 'Frailty' and 'Perioperative Care', 'Frailty' and 'Vascular Surgery', 'Frailty' and 'Geriatric Anesthesia', 'Frailty' and 'Prehabilitation', 'Prehabilitation' and 'Vascular Surgery'.

We included randomized controlled trials, cross-sec-

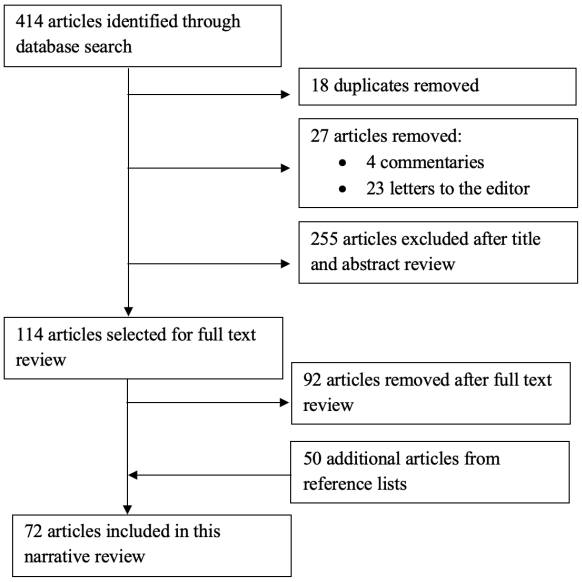

Figure 1 *Literature selection process in flowchart format*

tional and cohort studies. The most relevant reviews and guidelines on the subject were also included. Most relevant selection criteria were: performance of frailty assessment tools regarding postoperative outcomes; impact of perioperative interventions on postoperative outcomes; relevance of frailty assessment in vascular surgery setting; specific frailty assessment tools for vascular surgery patients and perioperative measures designed for these patients. Duplicates, commentaries, and letters to the editor were excluded. Articles non-related to frailty were excluded as well as articles thar refer to non-vascular surgery patients. Of the 414 articles initially identified, 18 duplicate articles were excluded. 27 publications were removed according to article type. Following abstract and title review, 255 articles were also excluded. After full text review, 92 publications were removed. Reference lists of the selected articles were searched for additional relevant publications related to frailty in vascular surgery and 50 articles were additionally included in this review. Two authors independently assessed the identified titles, abstracts and full texts. In total, 72 articles were included in this narrative review. The article selection process is revealed in Figure 1.

DISCUSSION

Concept of frailty

Frailty is an aging-related syndrome of physiological decline, however chronological age itself does not define frailty. Although the definition is not completely established, most experts consider it a multidimensional syndrome characterized by decreased reserves that leaves an individual vulnerable to adverse outcomes due to decreased tolerance of physical, physiologic or psychosocial stressors.[4]

Currently there are two main concepts of frailty: the phenotype model, originally defined by Linda P. Fried et al.[7] and the accumulating deficits model defined initially by Kenneth Rockwood et al..[8] The phenotype model (physical or syndromic frailty) includes signs and symptoms of fatigue, low activity, weakness, weight loss and slow gait.[7] The concept of deficit accumulation (index frailty) includes a combination of comorbidities, social situations and disabilities.[8] In both concepts frailty is associated with advanced vulnerability.

Irrespective of the chosen model, one must understand frailty not as a dichotomous concept, but rather a graded condition where higher levels of frailty represent greater vulnerability and risk of adverse outcomes.

Assessment tools for frailty

According to its nature, frailty cannot be quantified by a single measurement. Instead, its assessment requires multimodal indexes. For instance, the gold standard of frailty evaluation is a comprehensive geriatric assessment, which includes an extended review of medical, psychosocial, and functional status and limitations, followed by a set of interventions to reduce vulnerability levels.[15] However it takes from 60 to 90 minutes to perform, which renders it impractical in the perioperative setting.

Nowadays, there are multiple instruments to assess frailty.[9] However, many are too complex and time-consuming, making them unsuitable for perioperative teams.[10]

Five frailty instruments have the most robust evidence[11]: the Fried phenotype (FP)[7] based on the frailty phenotype concept; the Frailty Index (FI)[8] which represents the accumulating deficits concept; the Clinical Frailty Scale (CFS);[12] the Risk Analysis Index (RAI)[13] and the Edmonton Frail Scale (EFS).[14]

The FP is a 5-point scale which encompasses gait speed, hand grip strength, unintentional weight loss of >10 pounds during one-year, low physical activity, and exhaustion.[7] It takes around 10 to 20 minutes to complete and requires a handheld dynamometer, characteristics less suitable for preoperative context.[11,15]

The FI includes evaluation of a minimum of 30 deficits that also reflect multidimensional domains.[8] Its completion requires on average 12.5 minutes, making it less practical in a perioperative setting.[16]

The CFS is scored between 1 (very fit) and 9 (terminally ill) based on self-report of comorbidities and the need for help with activities of daily living.[17] One of the main advantages is its feasibility (around 1 minute to complete and no specific equipment required) without compromising accuracy[11] making it a valuable option not only for elective surgery but also emergency context.[18] In the United Kingdom, the Centre for Perioperative Care guidelines recommend the use of the CFS for preoperative frailty assessment.[19] Additionally, a recent systematic review concluded that CFS is one of the most studied tools and should be regarded as a well validated scale in the vascular surgery setting.[20]

The RAI is composed of 14 deficits related to demographic, comorbid, oncologic and disability states.[13] In a recent study, RAI was an ineffective predictor of 30-day morbidity and mortality for patients undergoing high-risk operations.[21]

The EFS assesses nine domains which are based on key aspects of comprehensive geriatric assessment and the patient is rated on a scale ranging from 0 to 17. It takes around 5 minutes to complete.[14]

Additionally, there is a shorter version of the FI, which is the Modified Frailty Index (mFI). There is an older version which includes 11 deficits and a more recent that includes 5 items.[22] The mFI has been particularly used in vascular surgery setting[23] mainly to predict postoperative complications after abdominal aortic aneurysm repair surgery[24] but also after carotid endarterectomy [25] due to its convenience of use.[26] However, it lacks precision to diagnose frailty and it should be regarded as a comorbidity index rather than a frailty screener (for example, any patient with hypertension, diabetes, and coronary artery disease would be classified as ''frail'').[23,27]

There is also evidence that the Groningen Frailty Indicator (GFI) and the modified Essential Frailty Toolset (mEFT) perform well among vascular surgery patients, particularly patients with peripheral arterial disease.[23] The GFI is a 15-point score that encompasses mobility, vision, hearing, weight loss, comorbidities, cognitive impairment, mental health, and physical fitness. The mEFT is a 5-point scale that encompasses lower extremity muscle weakness, cognitive impairment, anemia, and hypoalbuminemia.[23]

There is also worth mentioning a few scores specifically designed for vascular surgery patients: Addenbrooke's Vascular Frailty Score (AVFS)[28], Ruptured Aneurysm Frailty Score (RAFS),[29] Vascular Quality Initiative Frailty Score (VQI-FS)[30] and a specific risk score designed for patients submitted to Endovascular Repair of Descending Thoracic Aortic Aneurysms (the variables included are: functional dependence, pulmonary disease, thoracoabdominal extent, need for iliac access and zone I or II deployment).[31] AVFS is a 6-point scale that includes mobility, depression, polypharmacy, anemia, emergency admission, and risk of pressure ulcers. The AVFS is a good predictor of 12-month mortality, readmission, duration of hospital stay and discharge destination following vascular surgery procedures.[28] RAFS is a 9-point scale that encompasses functional independence (Katz score $\geq$6), anemia (hemoglobin level $<$102 g/L), comorbidities (Charlson score $>$1), polypharmacy ($>$5 medications on admission), visual impairment, absence of hearing impairment, and not taking a statin preoperatively. The RAFS accurately predicts 1-year mortality after ruptured abdominal aortic aneurysm repair. [29] The VQI FS score includes 7 variables (congestive heart failure, renal impairment, chronic obstructive pulmonary disease, not living at home, not ambulatory, anemia and underweight status) in addition to procedure-specific risk and it has shown strong correlation with postoperative 9-month mortality.[30]

Literature does not clarify which frailty screener should be used in perioperative setting. However, since the association of different frailty instruments with most relevant outcomes does not differ substantially, perioperative teams should strongly consider feasibility as a key factor. Even though data is limited, it consistently identifies the CFS as a quite practical tool, not time-consuming and simple (does not require special equipment).[11]

Regarding vascular surgery patients, particularly patients with lower extremity artery disease, physicians should be aware of the interference of the disease on their physical ability. Thus, this group of patients should not be evaluated with frailty screen tools focused on lower extremity physical performance. Critical Limb Ischemia Frailty (CLI Frailty) is an example of a frailty index specifically designed towards these patients. One individual is defined as frail through the CLI Frailty Index according to the Geriatric Nutritional Risk Index, skeletal muscle mass index and ambulatory status. This Index is useful in predicting the two-year overall survival of patients with CLI after infrainguinal revascularization.[33] More specific scales should be designed towards this population.[6]

Frailty and vasculopathy

As previously mentioned, the prevalence of frailty in vascular surgery patients is around 20 to 60%.[6] A high variability is related to the heterogeneity of the studies and the different scales used to identify frail patients. For example, in a systematic review and meta-analysis, prevalence of frailty was 49% in patients with lower extremity peripheral artery disease, but data revealed wide range of prevalence related to evaluation tools (for instance, modified FI-11 estimated 51% prevalence and CFS estimated 54% prevalence).[34] In spite of this issue, there is no doubt that frailty is highly prevalent among vascular patients.[35]

In addition, similar to findings in other surgical settings, frailty is associated with postoperative complications in patients submitted to vascular surgery: threefold increased 30-day mortality risk and twofold increased all-cause mortality, 30-day morbidity, reduced 2-year amputation free survival, greater number of major adverse cardiovascular events, graft/prosthesis/flap failure, Clavien-Dindo class IV complications, greater incidence of infection, adverse functional outcomes and cognitive impairment.[6,36] Regarding individual surgical groups, evidence extends to nearly all branches of vascular surgery, although the largest amount of data lies with lower limb peripheral vascular interventions. A recent meta-analysis revealed increased postoperative all-cause mortality both short and long term for frail patients with lower extremity peripheral artery disease.[37]

Incorporating frailty alongside clinical risk factors in the evaluation of vascular patients may provide better preoperative stratification of procedural risks and empower clinicians to match the procedure to the patient or, alternatively, to determine when a procedural intervention is likely to be futile.[36]

Frailty syndrome can also occur because of complex and stressful vascular surgeries. Efforts are needed to reduce the length of stay, the number of readmissions and the time required for recovery. Clinicians should understand frailty as a dynamic status. Therefore, pre-frail patients may develop multisystemic physiological decline and evolve to an irreversible frail status. On the other hand, with the implementation of goal-directed preoperative interventions, this deterioration might be prevented.

Preoperative frailty assessment is recommended by the Enhanced Recovery After Surgery (ERAS) Society for both lower

extremity vascular bypasses and open aortic vascular surgery. For patients with a high level of frailty, a comprehensive geriatric assessment with personalized intervention is advised and can also serve as a guide in therapeutic decision-making.[38,39]

Indirect estimations of frailty in vascular patients

Due to the lack of consensus on the definition of frailty, an effort has been made to find other parameters as an estimation of frailty.[40] These parameters include sarcopenia, motor performance and functional dependency. Sarcopenia is defined as a progressive quantitative and qualitative loss of muscle mass and it is a precursor of frailty.[41]

There are multiple tests to assess sarcopenia, from least to most accurate: calf circumference; psoas muscle area from a computed tomography scan; estimation of lean body mass from a bioimpedance device; and finally, total body muscle mass from a dual X-ray absorptiometry scanner.[6]

The literature has shown that sarcopenia is an independent prognostic indicator for short- and long-term mortality in hospitalized patients[42] and there is also evidence regarding vascular surgery patients. In fact, the psoas muscle area has been found to be an independent predictor of all-cause mortality after open and endovascular abdominal aortic aneurysm repairs.[43] In spite of the encouraging data, one should be cautious when interpreting it. Sarcopenia is by no means equal to frailty, which is a much wider concept. There are several limitations to each test and there is still a lack of evidence regarding the use of sarcopenia to evaluate frailty.[41]

Motor performance may be assessed with physical tests such as gait speed test, which have high sensitivity (99%) but low specificity (64%) to diagnose frailty.[44] In vascular patients there is an additional confounding factor, which is arterial disease that may impair mobility and compromise evaluation of motor performance and functional capacity This is where muscle mass evaluation may be useful, as it bypasses physical limitations from arterial disease.[6]

Functional dependency may be also used as a marker of frailty. It is defined as an inability to carry out activities of daily living without help and it may be also used as a marker of frailty, although it is rather an undesirable consequence of the latter. Functional dependency reduces the likelihood of a positive postoperative outcome and it is associated with increased risk of death following vascular (both abdominal aortic aneurysm repair and lower extremity artery disease surgery) or general surgical procedures.[45]

These approaches are limited by a lack of multidimensionality. In other words, using an isolated measure of physical performance does not capture all aspects of frailty.

Perioperative optimization

Besides its prognostic value, frailty should be regarded as an actionable finding with therapeutic value.

Surgery induces high physiological and psychological stress in any individual. From an anesthetic and surgical point of view, preoperative identification of frail patients provides an opportunity to adopt different measures to improve perioperative outcomes and reduce morbidity and mortality associated with surgery.[46]

Perioperative teams may adopt measures to improve results for these patients. They may include preoperative optimization of medical comorbidities, enhanced surveillance for complications such as delirium and falls, nutritional supplementation, proactive physical rehabilitation before and after surgery, cognitive status and mental health enhancement which seem promising in the reduction of the level of frailty or even reverse the frail condition.[6,47]

Therefore, it is presumed that prehabilitation may improve perioperative results for these patients. There is already evidence that screening and interventions that modulate the frailty status reduce postoperative and other complications such as delirium, functional decline and reduce length of stay.[48,49]

Additionally, there is room for frailty friendly intraoperative, anesthetic, and postoperative options.

Physical performance

Exercise prehabilitation programs improve well-being, increase mobility, reduce the risk of falls and enhance performance of activities of daily living and improve perioperative outcomes.[50,51] Overall, improving physical status may reduce frailty levels even in the most vulnerable patients. Any type of physical activity, even low intensity such as yoga, has demonstrated beneficial effects in reducing functional disability[52] However, for individuals with fewer functional limitations, the most promising model so far seems to be to perform cardiovascular resistance training 3 times a week at least 2 weeks prior to surgery.[53,54]

Identification of functional capacity before surgery could help to select individuals who might benefit from interventions to improve physical function. A simple screening tool recently published to assess functional capacity before surgery is the (modified) Duke Activity Status Index (M-DASI).[55]

Nutrition

Poor nutritional status is common among frail patients awaiting vascular surgery and is associated with increased length of stay, impaired functional recovery, slower wound healing and delirium.[4,38,39]

Hypoalbuminemia, although not directly related to nutrition status but rather to a predominant catabolic status, is associated with higher morbidity and mortality after any vascular surgery procedure.[56,57]

There is a panoply of tools to assess nutrition. One of the most relevant assessment instruments is the Mini Nutritional Assessment which is the European Society for Clinical Nutrition and Metabolism (ESPEN) recommended tool to evaluate nutrition status among older adults, in hospital, community, long term care and rehabilitation.[58]

The use of preoperative nutritional supplements with added proteins and calories has demonstrated beneficial effects in elderly people[59] and is an essential component of prehabilitation programs.[48]

The ESPEN guidelines on Clinical nutrition and hydration in geriatrics recommend an energy intake of 30 kcal per kg per day and a protein intake of 1 g per kg per day.[60] They also rec-

ommend measures to prevent low-intake dehydration: older women should be offered at least 1.6L of drinks per day, while older men should be offered at least 2L of drinks each day.[60]

Specifically for surgical patients, ESPEN recommend a period of 7 to 14 days of nutritional support therapy prior to major surgery in patients with higher risk of undernutrition and increased catabolic activity (weight loss >10-15% within six months, body mass index <18.5 kg/m2, nutritional risk screening >5 or serum albumin <30 g/l (with no evidence of hepatic or renal dysfunction)).[61]

In surgical context, preoperative fasting is associated with hunger, thirst, and preoperative nausea and vomiting and should be minimized. Recent guidelines from American Society of Anesthesiologists recommend that healthy adults should drink carbohydrate-containing clear liquids until 2h before elective procedures requiring general anesthesia, regional anesthesia, or procedural sedation. The carbohydrates may be simple or complex. Up to 400 ml of clear liquids is considered an appropriate volume.[62]

Diabetes and glycemic control

Poor glycemic control is associated with adverse events even in patients without a diabetes diagnosis. All patients scheduled for arterial vascular surgery should have their preoperative glycated hemoglobin levels evaluated, and glycemic control therapy should be initiated when indicated. Glycated hemoglobin levels above 10% are associated with significant complications. During the perioperative period, both hypoglycemia and hyperglycemia should be avoided, with recommended glucose levels maintained between 140 and 180 mg/dL.[38,39]

Anemia screening and optimization

Preoperative anemia is linked to negative postoperative outcomes. Managing anemia preoperatively should begin 3 to 4 weeks before surgery. Correcting anemia preoperatively can reduce the need for transfusions, though there is little evidence of its impact on morbidity and mortality. For patients with existing anemia, minimally invasive techniques or systems such as cell savers should be considered to minimize the need for transfusions.[38,39] Studies on the correction of preoperative anemia and iron deficiency in vascular surgery are limited in the literature. Despite the scarcity of research, correcting iron deficiency regardless of preoperative hemoglobin levels may impact postoperative outcomes.[63]

Mental health and cognition

The diagnosis of a disease increases the level of anxiety and depression in patients. Furthermore, older adults are associated with an increased risk of neurocognitive dysfunction which increases the risk of delirium.[4]

More than one-third of vascular surgery patients suffer from depression. Major depression in these patients is associated with increased morbidity and mortality.[64] Regarding screening tools for depression in the perioperative setting, the 9-question Personal Health Questionnaire (PHQ-9) is a validated scale for depression.[64]

Regarding cognition, the Mini-Cog test remains recommended by different best practice guidelines and can be considered as a cognitive screener before surgery.[65] However, it has limited evidence for detecting mild neurocognitive disorders (NCD), which is a concern since mild NCD are associated with postoperative cognitive complications. In that regard, Montreal Cognitive Assessment (MoCA) is a more precise tool.[66]

There are few strategies implemented in this area. One strategy that has revealed beneficial effects was the implementation of occupational therapy with positive results in improving the performance of activities of daily living, social participation, cognition and disability.[67]

Preoperative depression screening and appropriate medical and psychological follow-up are recommended.[19,39]

Best practices to prevent delirium should also be implemented in the perioperative journey of each frail patient and are further discussed in the next section.

Intraoperative and postoperative frailty tailored options

Principles such as avoiding multiple centrally acting drugs, reducing opioid administration, and offering regional techniques should incorporate any anesthetic and analgesic plan for frail patients in order to reduce cardiovascular and pulmonary complications and the risk of delirium.[68]

Current evidence for delirium prevention suggest careful titration of anesthetic depth[69], avoid hypotension, avoid anticholinergic load, and provide adequate pain control. If an anticholinergic is necessary at some point, glycopyrrolate is preferrable to atropine.[68,70]

Intraoperative homeostasis is of vital importance. Goal-directed fluid therapy strategies aim to achieve the optimal balance between volume overload and fluid depletion, which may particularly benefit frail patients who are at higher risk of developing hemodynamic instability under anesthesia. Additionally, preventing intraoperative hypotension, defined as a 40% decrease from pre-induction mean arterial blood pressure lasting more than 30 cumulative minutes, is crucial for avoiding adverse outcomes in this patient population.[39,68]

Protective ventilation strategies should be considered. Monitoring neuromuscular blockade intraoperatively ensures adequate muscle relaxation and reduces the risk of postoperative pulmonary complications. Additionally, it ensures the complete reversal of neuromuscular blockade before extubation.[38,68] Hypothermia entails various associated complications, notably an increased risk of arrhythmias, coagulopathy, and heightened susceptibility to surgical wound complications.[38] Complications due to hypothermia can be increased in the frail population making temperature monitoring and strategies to maintain normothermia even more crucial in this patient population.[68]

Postoperative care should also be of concern, regarding high risk of postoperative complications. Postoperative pain should be managed with a multimodal and opioid-sparing approach, always including regional techniques if possible.

Strategies to prevent pressure ulcers are also important and include: early mobilization, adoption of positioning techniques which protect impaired musculoskeletal and integ-

umentary systems, such as lifting instead of sliding or the application of soft padding to potential pressure areas.[19,71]

Other measures that can reduce the risk of delirium are: the presence of a relative or carer in the anesthetic room and/or post anesthetic care unit, access to sensory aids in recovery and avoid the use of unnecessary urethral catheters.[19,71]

The post discharge period also represents a vulnerable time for frail patients, with high rates of adverse events.[72] In order to reduce morbidity and readmission rates, appropriate discharge instructions and follow up plans are mandatory and should involve support services and informal caregivers.

CONCLUSION

The aging of the population is a reality, which will lead to increased challenges for health professionals. Frailty is common among vascular surgery patients and increases the risk of negative post-operative outcomes, which entails costs for healthcare systems. The preoperative identification of patients with high vulnerability may improve risk stratification and guide individualized therapy for vascular surgery patients. It also represents an opportunity for optimization of the contributors to frailty which should be a concern for all clinicians. Available data is not able to identify a single best instrument, leaving this as an area for future research. Its accuracy and feasibility make the Clinical Frailty Scale one of the preferred options for preoperative screening. Recently have been developed specific assessment tools designed to vascular surgery patients such as AVFS, RAFS, CLI Frailty Index and VQI-FS. The last one seems particularly interesting due to the inclusion of procedure-specific risk.

To achieve meaningful prehabilitation, multidisciplinary approach is pivotal. Prehabilitation programs focused on improving functional capacity, nutritional status and mental health are showing promising results. Furthermore, specific intraoperative and postoperative measures are essential to reduce the risk of complications, to ensure an enhanced recovery after surgery and to improve overall perioperative outcomes.

Future research targeting frail individuals will be needed to establish the efficacy of prehabilitation and to determine the most relevant perioperative interventions.

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