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Research Progress of Postoperative Recurrence of Chronic Subdural Hematoma in Chinese and Western Medicine

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Abstract: ***This review summarizes the risk factors associated with recurrent CSDH, including patient-specific factors, imaging factors, surgical factors, and pharmacological factors, while exploring the mechanisms underlying CSDH recurrence from the perspective of Traditional Chinese Medicine (TCM) theory. Aging is inextricably linked to CSDH, and the integration of TCM and Western medicine, along with anti-aging strategies, represents an effective approach to preventing CSDH recurrence.***

Keywords: Chronic subdural hematoma, Recurrence, Risk factors, Traditional Chinese medicine, Vascular aging.

1. Introduction

Chronic subdural hematoma (CSDH) is a prevalent neurosurgical condition with an incidence rate ranging from 1/100, 000 to 15/100, 000. It predominantly affects elderly patients, with an annual incidence of up to 48/100, 000 [1]. The abnormal accumulation of intracranial hematoma between the dura mater and arachnoid membrane compresses brain tissue, often causing symptoms such as dizziness, headaches, and chronic increased intracranial pressure, as well as neurological deficits like impaired limb function. In elderly patients, cognitive changes and consciousness disorders are more frequently observed [2]. Surgical intervention is the primary clinical treatment [3], and symptoms can be rapidly alleviated after hematoma evacuation.

However, the recurrence rate of this condition, as high as 20-26%[4], significantly increases the economic and physical/mental burden on patients. Clinically, CSDH recurrence is defined as a postoperative follow-up cranial CT scan within 3 months showing increased subdural fluid volume, accompanied by aggravated clinical symptoms such as dizziness and headache, neurological deficits, or even altered consciousness status [5]. This article reviews the recurrence of CSDH in elderly patients from aspects including patient factors, imaging classification, surgical approaches, and pharmacological treatment. It also explores the pathological mechanisms of CSDH and the positive role of traditional Chinese medicine (TCM) in preventing recurrence from the perspective of TCM theory, providing reference for clinical integrated TCM-Western medicine treatment of CSDH patients.

2. Factors Associated with CSDH Recurrence

2.1 Patient Factors

Age is closely associated with the recurrence of CSDH, with elderly patients exhibiting a higher recurrence rate compared to younger individuals [6]. Qian et al. [7] demonstrated a correlation between advanced age and elevated recurrence rates through statistical analysis of 242 patients who underwent burr hole drainage. Cerebral atrophy is a risk factor for both the onset and recurrence of CSDH [8]. Elderly patients generally present with cerebral atrophy, resulting in a larger interarachnoid space compared to younger individuals. This leads to slower and less pronounced postoperative brain tissue bulging, thereby increasing the likelihood of CSDH recurrence. In addition to age, gender is also an independent factor for CSDH recurrence. Studies have shown that male patients have approximately twice the postoperative recurrence rate compared to female patients [9]. Underlying conditions typically influence the prognosis of other diseases, and this applies equally to CSDH recurrence. Conditions such as diabetes, cardiovascular disease, malignancies, and osteoporosis can all contribute to postoperative CSDH recurrence [10-11].

Elderly patients typically take antithrombotic medications (including anticoagulants and antiplatelet drugs) for disease prevention. Studies have shown [12] that the use of antithrombotic drugs is associated with a high recurrence rate of CSDH, increasing the risk of reoperation in CSDH patients without increasing the risk of death. Additionally, a meta-analysis indicated that the use of antiplatelet drugs has a statistically significant impact on CSDH recurrence, while the use of anticoagulants has a borderline significance [13]. The influence of anticoagulants and antiplatelet drugs on CSDH recurrence remains a controversial topic. Another study [14] suggested that the association between the use of any type of anticoagulant or antiplatelet drug and the occurrence of recurrence is not statistically significant.

Preoperative or postoperative laboratory parameters can also reflect the recurrence of CSDH. Eagle [15] et al. conducted a statistical analysis of platelet counts at admission in 87 CSDH patients, revealing that approximately 26% of patients with admission platelet counts $<157\times10^9$/L experienced postoperative recurrence, while the remaining patients with admission platelet counts $>313\times10^9$/L showed no recurrence postoperatively. This difference was statistically significant, indicating that admission platelet count is a predictive factor for CSDH recurrence. A retrospective analysis of the correlation between lipid levels and CSDH recurrence rate demonstrated that low high-density lipoprotein (HDL-C) levels were significantly associated with recurrence of chronic subdural hematoma [16]. A study on the impact of cholesterol-lowering drugs on postoperative CSDH recurrence supported this view, showing that higher HDL-C levels were associated with lower recurrence and the likelihood of repeat surgery [17]. Matsubara [18] et al. emphasized the need for careful follow-up of CSDH patients with elevated preoperative peripheral blood eosinophils, noting that isolated eosinophils in differential white blood cell counts were significantly correlated with CSDH recurrence. The Prognostic Nutrition Index (PNI=5 × lymphocyte count + serum albumin concentration) serves as a baseline marker for nutrition and inflammation, playing a critical role in predicting the prognosis of many diseases. Zhu [19] et al. analyzed PNI levels in peripheral blood of discharged CSDH patients and found that low PNI levels were associated with an increased risk of CSDH recurrence. The study by Wang et al. [20] demonstrated that elevated postoperative blood urea nitrogen (BUN) levels were associated with recurrent CSDH within 3 months, whereas creatinine (Cr) levels showed no correlation with recurrence.

2.2 Imaging Factors

CSDH is typically diagnosed via CT scan, with bilateral hematoma, preoperative hematoma thickness, and significant midline shift being independent risk factors for CSDH recurrence [21]. As early as the beginning of the 21st century, Nakaguchi [22] classified CSDH into four types — homogeneous, laminated, separated, and reticular—based on hematoma density and internal structure as shown on CT images. Miah et al. [23] found that patients with laminated or separated hematoma structures often had a higher postoperative recurrence risk; among the four types of CSDH, those with mixed or high-density hematomas exhibited a greater postoperative recurrence risk. Postoperative CT scans after CSDH evacuation revealed the superficial layer of residual hematoma and the deep layer between the superficial and deep layers of residual hematoma, termed the biconcave sign. Miki [24] retrospectively analyzed data from 278 CSDH patients treated with single-port craniotomy and concluded that the detection of the biconcave sign within 7 days postoperatively was an independent predictor of chronic subdural hematoma recurrence. Jang et al. [25] calculated the volume of postoperative ventricular collapse in CSDH patients using CT imaging and identified a postoperative ventricular collapse volume >50 cm^3 visualized on CT scan within 7 days as a risk factor for CSDH recurrence.

Although CT is convenient, rapid, and accurate for diagnosing CSDH, MRI is more sensitive than CT in determining the internal structure of CSDH [26]. Neshige [27] et al. found that MRI imaging showing a laminated or dissecting hematoma is a risk factor for CSDH recurrence, which is consistent with the classification on CT imaging. Goto [28] et al. demonstrated that MRI T1 high-signal hematomas are considered to represent more mature and stable hematomas, associated with a lower recurrence rate; the recurrence risk in the T2 iso/low-signal group is more than five times higher compared to the T2 high-signal group.

2.3 Surgical Factors

2.3.1 Drilling Drainage

Burr-hole craniostomy (BHC) [29] is one of the most commonly used surgical procedures for treating chronic subdural hematoma (CSDH). It is typically performed under general anesthesia, involving drilling a hole in the skull, incising the dura mater, and irrigating with normal saline, followed by the placement of a drainage tube for continuous drainage for 1-3 days.

The number of drilling sites has long been a contentious issue. Some studies [30] indicate that single-drilling treatment for cSDH results in longer hospital stays, higher wound infection rates, and increased postoperative recurrence rates, while others [31] argue that single-drilling surgery offers advantages such as shorter duration, minimal trauma, and lower postoperative complications. For large cSDH cases, some clinicians opt for drilling two sites. A meta-analysis [32] demonstrated no significant difference between single-drilling and double-drilling surgeries in terms of postoperative complications and recurrence rates. However, for patients with bilateral cSDH, double-drilling drainage is deemed essential, as research shows [33] that the recurrence risk in cases treated with unilateral surgery is twice that of bilateral surgery.

Regarding intraoperative irrigation, some studies suggest [34] that irrigating hematoma fluid with normal saline during surgery is unnecessary, as it may prolong operative time and increase infection risks. Moreover, there was no statistically significant difference in postoperative recurrence rates compared to the non-irrigated group. However, a recent multicenter, randomized, controlled, and observational study conducted in Finland [35] demonstrated that not performing saline irrigation after drilling drainage does not result in non-inferiority. Furthermore, the non-irrigated group exhibited a 6.0 percentage point higher rate of reoperation compared to the irrigated group.

Regarding postoperative drainage tube placement, studies have demonstrated that drainage after surgery is effective in reducing the recurrence of CSDH symptoms, with no strong evidence suggesting that drainage increases any complications. Regarding the choice of drainage tubes, one study found that closed drainage for CSDH using mushroom-head drainage tubes and traumatic drainage tubes showed no statistically significant differences in hematoma clearance rate, clinical improvement, or recurrence risk. The placement site of drainage tubes also varies. A multicenter, prospective, randomized, controlled trial revealed that subperiosteal drainage offers advantages over the commonly used subdural drainage, including lower rates of drainage tube misplacement, reduced surgical infection risk, and lower recurrence rates. A meta-analysis indicated that the choice between subperiosteal and subdural drainage does not significantly affect the prognosis of CSDH, highlighting subperiosteal drainage as an alternative treatment option for CSDH. Anagnostopoulos et al. demonstrated that valve-controlled drainage after CSDH surgery can reduce the recurrence of postoperative pneumocephalus and hematoma, serving as an effective and safe alternative.

2.3.2 Minimally Invasive Puncture and Drainage

Minimally invasive puncture drainage (versus twist-drill craniostomy, TDC) [41], performed under local anesthesia, is characterized by short operative time and minimal scalp trauma, making it the preferred surgical option for elderly patients with compromised cardiopulmonary function. The puncture site is typically located around the parietal tubercle or at the thickest hematoma as identified by CT. Under local anesthesia, a 0.3cm incision is made at the puncture site using a scalpel. A disposable Y-1 intracranial hematoma crushing needle is inserted into the hematoma cavity via an electric drill, followed by removal of the needle core and connection to a drainage device. The site is then irrigated repeatedly with saline until the irrigation fluid becomes pale bloody [42].

The debate over whether minimally invasive TDC or BHC is the optimal surgical approach for treating CSDH remains unresolved. A multicenter prospective randomized trial demonstrated [43] that both techniques effectively treat CSDH patients with comparable 6-month outcomes, though BHC exhibits the lowest recurrence rate and manageable complication incidence. Another study [44] found no significant difference between the two procedures in clinical symptom improvement or CT imaging enhancement, positioning TDC as a viable alternative to BHC for CSDH management. A meta-analysis by Yagnik et al. [45] compared the hematoma evacuation rates of primary CSDH between the two techniques, revealing no clear superiority of either, but noting higher postoperative recurrence rates with TDC. The use of negative pressure drainage in TDC may result in recurrence rates comparable to those of BHC.

Some scholars have suggested that combining TDC with intrathecal urokinase injection can significantly reduce postoperative residual hematoma and lower the recurrence rate of CSDH [46]. Urokinase, an endogenous fibrinolytic agent, accelerates hematoma dissolution, effectively degrades deposits within the hematoma cavity and drainage tubes, enhances drainage efficacy, thereby reducing recurrence. Chen [47] et al. performed TDC combined with intrathecal urokinase injection in 697 CSDH patients, achieving a clinical cure rate of 85.08% and a recurrence rate of 7.6%, which is worthy of promotion by clinicians.

2.3.3 Other Procedures

The large bone flap craniotomy for hematoma evacuation [42] enables more direct and thorough removal of blood clots with lower recurrence rates postoperatively. However, this approach involves significant trauma and carries higher risks of complications, making it primarily indicated for refractory chronic subdural hematoma (CSDH) with severe tissue scarring. Small bone flap craniotomy demonstrates comparable efficacy in reducing CSDH recurrence rates and may serve as an alternative to large bone flap procedures [48]. A case report by Zhu et al. [49] highlighted a successful treatment of recurrent CSDH patients through craniotomy with multiple bone flap perforations and repositioning, achieving complete resolution without recurrence. This innovative surgical strategy provides a novel therapeutic option for refractory CSDH.

Neurosurgical-assisted hematoma evacuation can more effectively separate the dura mater and endometrium, reducing the recurrence rate of CSDH [50], and can be applied in both HBC and craniotomy for hematoma evacuation. An analysis by Mata [51] demonstrated that the recurrence rate and risk of complications were significantly reduced after endoscopic-assisted surgery.

In the selection of neuroendoscopes [42, 52], rigid endoscopes are more widely preferred due to their superior accessibility and image quality, as well as their multifunctional sheath. Although flexible neuroendoscopes offer greater convenience for multidirectional manipulation and avoid compressive injury to brain tissue caused by angle limitations, they exhibit poorer operability, thereby increasing the difficulty of surgical procedures.

Mandai et al. [53] first reported the use of middle meningeal artery (MMA) embolization to prevent recurrence of chronic subdural hematoma (CSDH) in 2000. The MMA is the primary blood supply vessel for CSDH formation. Embolic materials are delivered into the vessel via catheter-based interventional techniques to block blood flow. A multicenter study by Kan et al. [54] evaluated 154 cases of MMA embolization, with 9 patients experiencing recurrence. MMA embolization can also be combined with other surgical approaches for CSDH treatment. Sun et al. [55] demonstrated in a study on combined drilling-drainage and intraoperative MMA occlusion for CSDH that precise localization and occlusion of the MMA during surgical drilling-drainage, along with appropriate hematoma drainage, can reduce recurrence rates. This approach not only resolves the standing effect but also blocks the source of hematoma.

2.4 Pharmacological Factors

Due to the complex pathogenesis of CSDH, which remains unclear, this complexity has hindered the development of effective pharmacological treatments for CSDH. Atorvastatin, a traditional lipid-lowering drug with additional anti-angiogenic and anti-inflammatory effects, has become one of the commonly used medications for CSDH [56]. A meta-analysis on the efficacy and safety of atorvastatin in treating CSDH demonstrated [57] that atorvastatin may help reduce the recurrence of CSDH hematomas, with no significant association observed between atorvastatin and adverse events. Larger-scale, high-quality randomized studies are required to fully evaluate the efficacy, safety, and optimal dosage of atorvastatin in CSDH patients. Wang et al. [58] found no statistically significant effect of atorvastatin in preventing postoperative recurrence of CSDH. However, further clinical studies have shown that atorvastatin alone or in combination with surgery can effectively improve the prognosis of CSDH and reduce the postoperative recurrence rate [59].

Dexamethasone, a potent anti-inflammatory agent, has also been employed in the treatment of chronic subdural hematoma (CSDH). However, due to the numerous side effects associated with hormonal medications, the use of dexamethasone for CSDH management remains controversial.

A prospective randomized controlled trial demonstrated [60] that postoperative dexamethasone administration for two weeks showed no significant differences in neurological and radiological outcomes or mortality rates compared to placebo. Although the dexamethasone group exhibited a lower recurrence rate, it reported slightly higher complication rates, though these differences were not statistically significant. In contrast, a parallel, superiority, multicenter, pragmatic randomized controlled trial by Hutchinson et al. revealed that the dexamethasone group experienced higher rates of adverse outcomes and severe adverse events compared to the placebo group [61]. Gong [62] et al. found that dexamethasone enhances the anti-inflammatory and anti-angiogenic effects of atorvastatin by increasing its accumulation in hematomas and macrophages and modulating macrophage function. A meta-analysis of postoperative combined dexamethasone administration [63] indicated that surgical dexamethasone reduced the recurrence risk of CSDH compared to surgery alone, but did not improve overall mortality or functional outcomes.

Angiotensin-converting enzyme inhibitors (ACEIs) can regulate angiogenesis and play a role in reducing the recurrence of chronic subdural hematoma (CSDH) [64]. However, a multicenter study [65] showed that the use of ACEIs postoperatively for CSDH was not associated with a lower recurrence rate. Stejskal [66] and colleagues shared this view, finding that among 217 patients who underwent CSDH surgery, 79 continued to take ACEIs, while the remaining 138 did not. Statistical analysis revealed that the recurrence of CSDH did not appear to be influenced by the use of ACEIs.

Tromboxane A2 (TXA) is a safe and widely used fibrinolytic inhibitor. Lodewijkx [67] et al. demonstrated that TXA can be considered as the first-line pharmacotherapy for patients with mild CSDH symptoms. Yang [68] et al. found that the use of TXA as adjuvant therapy after CSDH significantly promoted the absorption of residual CSDH and led to early remission of CSDH, thereby reducing the recurrence rate. Yu [69] et al. conducted a Bayesian network meta-analysis of different pharmacotherapies for CSDH, which showed that atorvastatin combined with dexamethasone, atorvastatin, dexamethasone, and TXA had definite efficacy in improving recurrence in CSDH patients, but atorvastatin combined with dexamethasone was the optimal intervention for improving recurrence in CSDH patients.

3. Traditional Chinese Medicine and CSDH

3.1 Understanding of Traditional Chinese Medicine in the Recurrence of CSDH

CSDH (Cerebral Spinal Dystonia) is located in the brain and lacks a specific disease name in Traditional Chinese Medicine (TCM). It can be categorized under conditions such as "headache," "dizziness," or "stroke." TCM theory posits that CSDH generally falls under the syndrome of "deficiency of the root and excess of the branch," with blood stasis being the core TCM syndrome [70]. The pathogenesis is fundamentally attributed to essence deficiency and marrow depletion.

3.1.1 Deficiency of kidney essence and marrow depletion leading to cerebral atrophy are the fundamental causes of CSDH recurrence

Cerebral Spondylotic Dystonia (CSDH) primarily affects the brain, with a higher prevalence in elderly individuals. The degeneration of spinal cord and brain tissue provides ample space for CSDH development. Traditional Chinese Medicine (TCM) posits that all spinal cord components belong to the brain, which is referred to as the "Sea of Marrow" (Mai Hai) – the convergence point of vital essence. The brain is considered a vital organ, and its disorders often manifest as deficiency, particularly in essence, qi, and blood [71]. As stated in "*Ling Shu·Jing Mai*": "At birth, essence is first formed; upon its formation, brain marrow develops" [72]. With aging and physical decline, kidney essence becomes deficient, leading to depletion of essence and blood. This results in the marrow losing its source of transformation, causing insufficiency of the Sea of Marrow. Over time, this leads to atrophy of the brain orifices. Additionally, postnatal malnutrition weakens the spleen and stomach's ability to process food essence, further depleting the source of qi and blood. The deficiency of qi and blood causes blood vessels to become congested and sluggish, impairing upward circulation. Consequently, the brain loses nourishment and atrophies.

3.1.2 Damage to collateral vessels and blood stasis formation are key factors in the recurrence of CSDH

1) Deficiency of the Collaterals Caused by Deficiency of Essence

In his work "Clinical Guide to Medical Cases," Ye Tianshi [73] stated: "Yin collaterals are the collateral vessels subordinate to the viscera," and brain collaterals fall under the category of Yin collaterals. They participate in the distribution of qi and blood in the brain, serving as an essential component of the brain. When primordial qi is deficient, body fluids and essence are insufficient, and the blood collaterals and vessels fail to receive nourishment, leading to impaired lubrication. The normal pathways for blood circulation are compromised, creating conditions for the exudation of substances within the blood collaterals. Consequently, blood that should be functioning normally slowly seeps out, causing the collaterals to rupture and blood to overflow, resulting in blood that has deviated from its normal course.

2) Deficiency of Essence Leading to Collateral Stasis

The Treatise on Blood Disorders states: "Qi serves as the commander of blood, guiding its circulation; blood acts as the guardian of qi, enabling it to remain tranquil." [74] In elderly individuals with kidney essence deficiency, the essence fails to transform into qi, resulting in qi deficiency and inability to propel blood circulation. This leads to blood stasis in the body's blood vessels. Blood stasis further obstructs qi flow, causing qi to stagnate in the blood vessels and exacerbating the stasis. The Medical Forest Rectification notes: "When primordial qi is deficient, it cannot reach the blood vessels. Without qi in the vessels, blood stagnates and becomes stasis." [75] Deficient primordial qi impairs qi's ability to hold blood. When qi fails to retain blood, blood leaks outside the vessels, forming stasis. The Medical Guide explains: "When deficiency cannot control water... water overflows and becomes phlegm." [76] In the elderly, kidney essence deficiency weakens the yang qi in the kidneys, reducing its evaporation function and impairing qi transformation. This disrupts fluid metabolism, leading to phlegm. With age and physical decline, acquired malnutrition weakens the spleen's function, impairing the transformation of food essence. Abnormal distribution of body fluids and impaired water metabolism result in phlegm. Intangible phlegm and turbidity accumulate in the brain and blood vessels, eventually affecting qi and blood circulation, forming stasis. Phlegm and stasis mutually influence, cause, and bind each other. Blood stasis in the vessels prevents body fluids from accompanying blood flow, accumulating into phlegm. The interpenetration of body fluids and blood causes water stagnation, suppressing yang qi and disrupting blood circulation, leading to stasis.

In the pathogenesis of CSDH, deficiency of collateral vessels and stagnation of collateral vessels ultimately lead to collateral vessel damage and instability. Essence deficiency and collateral vessel damage are inseparable, with "essence deficiency" rooted in kidney essence deficiency and deficiency of primordial qi, and "collateral vessel damage" manifested as collateral vessel impairment and blood stasis. The two are mutually causal, dynamically evolving, and jointly driving the progression of CSDH.

3.2 Prevention and Treatment of CSDH Recurrence with Traditional Chinese Medicine

Traditional Chinese Medicine (TCM) for the prevention and treatment of CSDH is not only theoretically feasible but also demonstrates favorable clinical outcomes. A meta-analysis [77] revealed that TCM is effective and safe in treating CSDH, reducing the risk of recurrence. Cross-sectional studies [78] have shown that the rational application of blood-activating herbs in TCM treatment, combined with syndrome differentiation and individualized medication adjustments, not only prevents exacerbation of bleeding but also promotes hematoma absorption, accelerates hematoma resolution, and rapidly alleviates patient symptoms. A clinical efficacy observation of surgical treatment combined with blood-activating and stasis-resolving methods for CSDH [79] demonstrated that medications with blood-activating and stasis-resolving effects can improve postoperative clinical outcomes, enhance neurological function, and increase daily living capacity. Research by Professor Fan Xiaoxuan's team [80] found that adding Peiyuan Huayu Decoction to conventional Western medical treatment for CSDH patients on the 7th day after drilling and drainage significantly outperformed the Western medicine-only group in improving clinical symptoms and promoting residual blood volume absorption.

4. Summary

The pathogenesis of CSDH is complex and not yet fully elucidated, involving cerebral injury-induced bridging vein rupture, inflammatory responses, and angiogenesis [35]. Although there is controversy among scholars regarding the mechanisms of CSDH, it is an indisputable fact that CSDH has become an age-related disease [81].

Inflammatory aging and systemic inflammatory states may provide intrinsic conditions for the expansion and recurrence of chronic suppurative skin disease (CSDH) [82]. Senescent cells exhibit strong secretory activity, secreting various factors such as pro-inflammatory factors, chemokines, growth factors, and matrix metalloproteinases (MMPs) into the extracellular space, a phenomenon termed the senescence-a ssociated secretory phenotype (SASP) [83]. The increased secretion of SASP exacerbates the body's inflammatory response. Studies have found [84] that SASP expression is closely associated with CSDH recurrence, with significantly elevated levels of IL-6, IL-8, VEGF, and MMP-9 observed in patients with recurrent CSDH.

Vascular aging is particularly prominent in the aging process of the human body [85], primarily manifested as thickening of the vascular wall, decreased vascular elasticity, and microvascular thinning. Vascular aging may be closely associated with the occurrence and recurrence of CSDH [86]. During vascular aging, endothelial cell damage and increased vascular permeability predispose to microvascular leakage, thereby promoting the onset and progression of CSDH.

Therefore, personalized strategies for preventing recurrence can be formulated based on individual patient factors and influencing factors. The selection of surgical approaches can also effectively reduce recurrence rates. Given that most CSDH patients are elderly, regulating systemic inflammation levels and preventing vascular aging may represent a novel strategy for preventing CSDH recurrence, which aligns with the Traditional Chinese Medicine (TCM) theory of "deficiency of essence and damage to collaterals." Postoperative combined treatment of CSDH with integrated Chinese and Western medicine is an effective method for preventing CSDH recurrence, bringing hope to a wide range of CSDH patients.

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