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MODERN ASPECTS OF OPTIMIZING THE SURGICAL TREATMENT OUTCOMES OF ISCHEMIC MITRAL VALVE INSUFFICIENCY

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The purpose of the study was to develop a clinical-diagnostic algorithm for determining surgical indications and choosing surgical methods for ischemic mitral valve insufficiency, aiming to improve short- and long-term outcomes. The two groups were involved: Group I (main) consisted of 132 patients who underwent surgery for ischemic mitral valve insufficiency between 2014 and 2020 using the proposed algorithm. Group II (comparison) consisted of 65 patients who underwent surgery for ischemic mitral valve insufficiency based on standard treatment protocols. In both groups, 79 % of patients were aged 51–60. Using identified potential predictors, an algorithm was developed to determine surgical indications and select the type of surgery for ischemic mitral valve insufficiency, which was then applied. According to results, over five years, survival in the algorithm group was 86.72 %, compared to 83.6 % in the comparison group (3.12 % lower). A comparative evaluation confirmed the effectiveness of the developed algorithm.

Key words: ischemic mitral valve insufficiency, diagnostic algorithm, surgical treatment, ischemic heart disease, five-year survival rate.

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СУЧАСНІ АСПЕКТИ ОПТИМІЗАЦІЇ РЕЗУЛЬТАТІВ ХІРУРГІЧНОГО ЛІКУВАННЯ ІШЕМІЧНОЇ НЕДОСТАТНОСТІ МІТРАЛЬНОГО КЛАПАНА

Метою дослідження була розробка клініко-діагностичного алгоритму визначення показань до хірургічного лікування та вибору методів хірургічного лікування ішемічної недостатності мітрального клапана з метою поліпшення найближчих і віддалених результатів. Було включено дві групи: I група (основна) складалася зі 132 пацієнтів, яким у період із 2014 до 2020 року було проведено операцію з приводу ішемічної недостатності мітрального клапана з використанням запропонованого алгоритму. II група (порівняння) складалася з 65 пацієнтів, яким було проведено операцію з приводу ішемічної недостатності мітрального клапана на основі стандартних протоколів лікування. В обох групах 79 % пацієнтів були віком 51–60 років. З використанням виявлених потенційних предикторів було розроблено алгоритм визначення показань до хірургічного втручання і вибору виду операції за ішемічної недостатності мітрального клапана, який потім було застосовано. Згідно з результатами, за п'ять років виживаність у групі алгоритму становила 86,72 % порівняно з 83,6 % у групі порівняння (на 3,12 % нижче). Порівняльна оцінка підтвердила ефективність розробленого алгоритму.

Ключові слова: ішемічна недостатність мітрального клапана, діагностичний алгоритм, хірургічне лікування, ішемічна хвороба серця, п'ятирічне виживання.

Ischemic heart disease (IHD) is one of the most frequent causes of heart failure: in 2020, approximately 18 million people worldwide were diagnosed with ischemic heart disease. In Europe, 47 % of annual deaths are due to IHD [7]. Among the causes of death in IHD, ischemic mitral valve damage is one of the most common. Previous myocardial infarction (MI) leads to ischemic mitral valve insufficiency (IMVI) in 33.65 %–40 % of cases [11]. IMVI is diagnosed in 3–5 % of patients with IHD, and conservative treatment is ineffective in 16.7 % of cases, necessitating surgical correction. The main challenge in treating IMVI is assessing the severity of the pathological process, identifying its mechanisms, and selecting an individualized surgical strategy [9, 12].

The treatment tactics for patients with moderate IMVI remain a topic of discussion. According to some authors, hospital mortality during combined treatment of coronary arteries (CA) and the mitral valve (MV) can reach 17 %. Coronary artery bypass grafting (CABG) alone does not improve valve function. For this reason, other clinicians consider MV repair more appropriate following revascularization in IMVI [2].

According to various studies, the five-year survival rate of IMVI patients ranges between 25 % and 69 % [14]. Major causes of death include drug-resistant heart failure, recurrent MI, and fatal ventricular arrhythmias. Although there is no consensus among cardiac surgeons on a precise strategy for IMVI treatment, currently, three types of surgical interventions are used: isolated myocardial revascularization (RV), RV+MV repair, and RV+MV replacement [11].

In mild (Grade I–II) IMVI, myocardial revascularization is considered the primary treatment; in moderate and severe cases, MV repair or replacement along with RV is recommended. However, these surgical methods do not address the core issue – left ventricular dysfunction [6].

Despite improvements, complications, recurrences, and mortality rates after all three surgical methods for IMVI remain a concern for clinicians. Indications for surgery and the choice of surgical technique are still under discussion and have not been definitively resolved [1].

The purpose of the study was to develop and apply a clinical-diagnostic algorithm to determine surgical indications and select surgical methods for ischemic mitral valve insufficiency, thereby improving short- and long-term surgical outcomes.

Materials and methods. The study was conducted in the period between 2014 and 2020 in the Scientific Surgical Center named after Academician M.A. Topchubashov. The two groups of patients were formed: Group I (main) included 132 patients who underwent surgery for IMVI between 2014 and 2020 using the proposed algorithm. Group II (comparison) included 65 patients who underwent surgery based on standard protocols. In the main group, out of 132 patients, 119 (90.2±2.59 %) were men and 13 (9.8±2.59 %) were women; in the comparison group, there were 58 (89.2 %) men and 7 (10.8 %) women. The average age in both groups was 51.8±7.01 years.

The inclusion criteria for the study were as follows: patients over the age of 35; diagnosed with Grade II or higher ischemic mitral valve insufficiency (IMVI) with coronary artery pathology; left ventricular ejection fraction ≤45 %; history of myocardial infarction within the past 6 months; ≥75 % stenosis of the left coronary artery or proximal stenosis of the left anterior descending artery; ≥75 % stenosis in two or more coronary arteries; and left ventricular end-systolic index (ESI) greater than 60 ml/m².

Exclusion criteria included: rheumatic or infectious heart valve disease; acute myocardial infarction, acute cerebrovascular accident, right ventricular failure, severe pulmonary hypertension not related to the mitral valve, mitral valve dysplasia, and rheumatic-origin pathologies.

Diagnostic procedures included electrocardiogram (ECG), transthoracic echocardiogram (TTE), transesophageal echocardiography (TEE), stress echocardiography, cardiac MRI, scintigraphy, and routine clinical-biochemical tests. The SF-36 questionnaire was used to assess quality of life (QoL).

Statistical analysis of the study results was performed using Statsoft Statistica 10 and Microsoft Excel 2016 software packages. All data were expressed as mean±standard error. Differences between groups for continuous and ordinal variables were determined using the Mann-Whitney non-parametric test; two-tailed t-test, one-way ANOVA, and Tukey's multiple comparison test were analyzed using GraphPad Prism version 7. For evaluating distribution types, the Kolmogorov-Smirnov criteria (with Lilliefors correction) were used, including quantitative variables in univariate analysis where asymmetry and kurtosis were not greater than 0.1. Shapiro-Wilk, Student, Mann-Whitney, Friedman, and Wilcoxon tests were used for applying variation statistics; Pearson (r) and Spearman coefficients were assessed. A p-value of less than 0.05 was considered statistically significant.

The study was approved by the Ethics Committee of the Scientific Center of Surgery (protocol № 01–3, dated 22.01.2021). All patients provided written informed consent to participate in the study voluntarily.

Results of the study and their discussion. In the main group, 71 (53.8±4.34 %) patients (67 men and 4 women) had a history of myocardial infarction, compared to 36 (55.4±6.17 %) patients (29 men and 7 women) in the comparison group. Hypertension was present in 67 (50.8±4.35 %) patients in the main group and in 34 (52.3±6.20 %) patients in the comparison group. Diabetes mellitus was found in 42 (31.8±4.05 %) patients in the main group and in 21 (32.3±5.80 %) patients in the comparison group. The types of mitral valve lesions, types of left ventricular dysfunction, degree of regurgitation, severity of clinical course, and frequency of pulmonary artery hypertension identified during examinations are presented in Table 1.

According to the NYHA classification, no patients in either group were in Functional Class I. Class II was observed in 31 (23.5±3.69 %) patients in the main group and 21.5±5.10 % in the comparison group; Class III included 65 (49.2±4.35 %) patients in the main group and 33 (50.8±6.20 %) in the comparison group; Class IV was present in 36 (27.3±3.88 %) patients in the main group and 18 (27.7±5.55 %) in the comparison group.

In the main group, the results of selective angiography were as follows: significant stenosis (≥70 %) in one vessel was detected in 9 patients (6.82±1.95 %), in two vessels – in 35 patients (26.51±3.46 %), and in three vessels – in 88 patients (66.67±4.15 %). In the comparison group, significant stenosis was found in one coronary vessel in 4 patients (6.15±2.98 %), in two vessels – in 18 patients (27.70±4.96 %), and in three vessels – in 43 patients (66.15±5.93 %) ($p>0.05$). Post-infarction remodeling (Di Donata) of grade I was observed in 29 patients (21.96±3.41 %) in the main group and in 13 patients (20.0±4.96 %) in the comparison group; grade II remodeling was found in 26 (19.60±3.24 %) and 12 (18.5±4.81 %) patients, respectively ($p>0.05$).

Table 1

Types of MV lesions, LV dysfunction, regurgitation levels, clinical severity, and frequency of pulmonary artery hypertension in the study groups

Indicators	Main group	Comparison group
Type of MV damage (A. Carpentier classification):		
Type I	15 (11.4±2.76 %)	8 (12.3±4.07 %)
Type II	41 (31.1±4.03 %)	21 (32.3±5.80 %)
Type III	61 (46.2±4.34 %)	29 (44.6±6.17 %)
Type IV	15 (11.4±2.76 %)	7 (10.8±3.84 %)
Level of regurgitation:		
Moderate	56 (42.4 %)	27 (41.5±6.11 %)
Moderate-to-severe	34 (25.8 %)	16 (24.6±5.34 %)
Severe	42 (31.8 %)	22 (33.9±5.87 %)
Type of LV dysfunction:		
Type I	46 (34.9±4.15 %)	23 (35.4±5.93 %)
Type II	40 (30.3±4.00 %)	19 (29.2±5.64 %)
Type III	46 (34.9±4.15 %)	23 (35.4±5.93 %)
Severity of clinical course:		
Type I (mild)	21 (15.91 %)	12 (18.46 %)
Type II (moderate)	39 (29.6 %)	25 (38.46 %)
Type III (moderate–severe)	32 (24.24 %)	28 (43.08 %)
Type of left ventricular diastolic dysfunction:		
I	47 (35.6 %)	22 (33.85 %)
II	50 (37.88 %)	25 (38.46 %)
III	35 (26.52 %)	18 (27.69 %)
Pulmonary artery hypertension (%)	54 (71.1 %)	46 (70.5 %)

In the examination groups, the main predictors identified were the type of MV lesion, type of LV dysfunction, level of regurgitation, severity of clinical course, and frequency of pulmonary artery hypertension. According to the A. Carpentier classification, type I MV lesion was found in 15 patients (11.4±2.76 %) in the main group and in 8 patients (12.3±4.07 %) in the comparison group; type II MV lesion in 41 (31.1±4.03 %) and 21 (32.3±5.80 %) patients, type III in 61 (46.2±4.34 %) and 29 (44.6±6.17 %) patients. We classified the condition of restricted posterior MV leaflet motion along with anterior leaflet prolapse as type IV MV insufficiency, observed in 15 patients (11.4±2.76 %) in the main group and in 7 patients (10.8±3.84 %) in the comparison group.

Moderate mitral regurgitation (MR) was observed in 56 patients (42.4 %) in the main group and in 27 (41.5±6.11 %) in the comparison group; moderate-severe MR in 34 (25.8 %) and 16 (24.6±5.34 %) patients, and severe MR in 42 (31.8 %) and 22 (33.9±5.87 %) patients, respectively. Grade I LV dysfunction was recorded in 46 patients (34.85±4.15 %) in the main group and in 23 (35.38±5.93 %) in the comparison group; grade II in 40 (30.3±4.00 %) and 19 (29.24±5.64 %), and grade III in 46 (34.85±4.15 %) and 23 (35.38±5.93 %) patients, respectively. Grade I LV diastolic dysfunction (LVDD) was observed in 47 patients (35.6 %) in the main group and in 22 (33.85 %) in the comparison group; grade II LVDD in 50 (37.88 %) and 25 (38.46 %) patients, and grade III LVDD in 35 (26.52 %) and 18 (27.69 %) patients.

Pulmonary artery hypertension was found in 54 patients (71.1 %) in the main group and in 46 patients (70.5 %) in the comparison group. These pathological changes exacerbated the clinical course of IMVI to varying degrees. Thus, mild clinical course (type I) was observed in 21 patients (15.91 %) in the main group and in 12 (16.92 %) in the comparison group; moderate (type II) in 24 (18.18 %) and 10 (15.38 %) patients, moderate-severe (type III) in 55 (41.67 %) and 28 (43.07 %) patients, and severe (type IV) in 32 (24.24 %) and 15 (23.07 %) patients, respectively.

In our study, the clinical severity of disease progression and the level of pathophysiological changes caused by IHD in patients with IMR in both the main and comparison groups confirmed the necessity of surgical intervention.

We considered it essential to develop an algorithm that could be easily used to determine surgical indications and the type of intervention based on existing knowledge of IMR, its pathogenesis, treatment strategies, clinical research and practical outcomes, and potential predictors. To this end, the most significant predictors from the following examination stages were used in creating the algorithm.

The first scale of the algorithm included: NYHA functional class of heart failure, percentage and number of coronary arteries with >70 % stenosis, severity of angina, troponin levels (ng/ml), cardiac index, radiological severity of pulmonary changes, and manifestation degree of comorbidities.

The second scale of the algorithm included: type of mitral valve lesion, severity of MR, LV ejection fraction, fibrous annulus diameter, type of LV dysfunction, levels of end diastolic diameter (EDD) and end

systolic diameter (ESD), vena contracta width, end-systolic index, leaflet coaptation depth and tenting, interpapillary muscle distance, cardiac index, effective regurgitant orifice area, left atrial size, severity of pulmonary artery hypertension, and percentage of scarred and asynergic segments. These criteria are independent of central hemodynamic changes and reflect the true degree of mitral valve dysfunction.

If at least 90 % of the parameters in scales I and II of the algorithms will matched, surgical intervention on the mitral valve was indicated. The cornerstone of pathogenetic treatment of IMR is myocardial revascularization. In patients with mild IMR (type I), NYHA class II, and a mild clinical course, isolated CABG was recommended. In patients with IMR presenting mild, moderate, or severe clinical courses and type III–IV mitral valve insufficiency due to left ventricular dysfunction, the choice of surgical procedure was guided by the third scale of the developed algorithm. This scale includes intraoperative predictors identified visually (ad oculus) and through TEE findings.

Predictors in Algorithm Scale III:

– Confirmation of type III and IV mitral valve lesion preoperatively+TEE signs:

– Grade II left ventricular remodeling;

– Severity of regurgitation;

– Significant discrepancy between leaflet and annulus plane;

– Chordae elongation, prolapse presence;

– Larger annular size (seen in ischemic cardiomyopathy);

– Damage to the posteromedial papillary muscle;

– Tethering of the posterior leaflet, ischemic prolapse;

– Scar-induced displacement of the posterior wall (aneurysmal dilation);

– Surgeon's intraoperative doubt on valve repair efficacy;

– Intraoperative signs of type IV IMR: signs of type III+anterior leaflet prolapse, posterior leaflet tethering, and significant plane discrepancy (anterior leaflet prolapse above annular level, posterior leaflet tethered below).

Based on this algorithm, the choice of reconstructive procedure along with CABG was determined by the following intraoperative criteria:

A) Ring Annuloplasty:

– A.1. Isolated Ring Annuloplasty (RA): indicated with distorted LV geometry and annular dilation. A support ring was chosen intraoperatively using a special sizing tool. Contraindications (valve calcification, immobility) were determined ad oculus.

– A.2. Ring Annuloplasty+Alfieri technique: used when water test after ring annuloplasty shows residual regurgitation.

– A.3. Ring Annuloplasty+Posterior Leaflet Augmentation: indicated if the tethering distance (from papillary muscle head to annulus) is large.

– A.4. RA+Quadrangular Resection: used if a small posterior leaflet prolapse is present; anterior leaflet prolapse, corrected by neochord implantation.

– A.5. RA+Dor procedure: for LV free wall aneurysm.

– A.6. RA+Neochord Implantation: in cases of annular dilation and anterior leaflet chordal elongation.

B) Isolated Three-Pledget Stitch Annuloplasty: used in high-risk patients to reduce pump and aortic cross-clamp time. Applied in moderate MR with intact anterior leaflet. The three pledgets reduce the mitral orifice: P1 adjusts transverse diameter, P2 and P3 adjust both transverse and anteroposterior diameters. Additional corrections (neochord, Alfieri stitch, resection) added based on water test.

C) CABG+Alfieri Stitch Valve Repair: used to minimize CPB and ACC time in high-risk patients where MR is expected to reduce to grade I–II. If so, procedure concluded.

II. Algorithm for Mitral Valve Replacement:

– Intraoperative signs of type III–IV mitral damage;

– ≥42.8±7.5 % of scarred segment;

– Annulus diameter ≥50.8±1.85 mm;

– Severe annular calcification in chronic dialysis patients;

– Grade II mitral calcification;

– Leaflet tethering: 1.3±0.1.

According to the algorithm, in the main group of 132 IMR patients: 25 (18.94 %) underwent isolated CABG; 77 (58.33 %) had mitral valve repair; 30 (22.73 %) had CABG+mitral valve replacement. In the comparison group of 65 patients: 22 (33.85 %) underwent isolated CABG; 33 (50.77 %) had mitral valve repair; 10 (15.38 %) had CABG+valve replacement.

Immediate outcomes: favorable results: 87.12 % in main group vs. 80.0 % in comparison group (5.6 % difference); satisfactory results: 0.2 % higher in comparison group; poor results: 2.32 % higher in comparison group. Postoperative mortality: 3.03 % in main group vs. 6.15 % in comparison group (3.07% difference). Outcome analysis: three-pledget stitch technique yielded favorable results in 82.35 % vs. 85.71 % for RA+additional techniques (difference 3.36 %); early mortality: 5.88 % for three-pledget vs. 4.76 % for RA+others (difference 1.12 %). Based on the third scale of the developed algorithm, using the three-pledget stitch technique in IMR surgery can be considered an appropriate approach.

In the early postoperative period, heart failure was observed in 43.2 % of patients in the main group and 44.6 % in the comparison group. Respiratory failure was noted in 14.4 % and 15.4 % of patients respectively. Cerebral circulation disorders occurred postoperatively in 3 (2.27 %) patients in the main group and 2 (3.08 %) in the comparison group. Arrhythmia developed in 24.2 % and 26.2 % of cases respectively. Atrial fibrillation was observed in 32 (24.2 %) patients in the main group and in 17 (26.15 %) patients in the comparison group.

Thus, although not statistically significant, the results of surgeries performed in patients with IMR according to our developed algorithm were numerically better than those performed in the comparison group. The number of good outcomes in the main group was 5.6 % higher; satisfactory outcomes were 0.2 % lower, and unsatisfactory results were 2.62 % lower than in the comparison group. Postoperative mortality was 3.03% in the main group and 3.12 % higher in the comparison group at 6.05 %. Intra-aortic balloon counterpulsation was required in 10 (9.8 %) patients in the main group and 5 (7.7 %) patients in the comparison group. According to the algorithm, 128 (96.97 %) of 132 IMR patients in the main group and 61 (93.84 %) in the comparison group were discharged in stable condition. Hence, although not statistically significant, the outcomes of surgeries performed based on our algorithm in IMR patients were numerically better than those in the comparison group.

Among the 128 patients discharged after different surgical interventions based on our algorithm for IMR, 111 (86.72 %) were alive at 5 years, while 17 (13.28 %) had died. In the comparison group, 51 (83.8 %) patients were alive at 5 years. Among the 17 patients who died in the main group over 5 years, the cause of death was identified in 9 (52.94 %) cases: progressive heart failure in 5, thromboembolic complications in 2, and severe oncological disease in 2 patients. Among the 9 (13.85 %) deceased patients in the comparison group over 5 years, causes were determined in 8: progressive heart failure in 4, thromboembolic complications in 1, and oncological causes in 1 patient. At the fifth postoperative year, 38 % of patients in the main group reported feeling well, 60% satisfactory, and 1.8 % poorly; in the comparison group, these figures were 36 %, 59 %, and 5 %, respectively. Their overall condition corresponded to NYHA Functional Class I–II. The average functional class at 5 years was 1.5±0.8 in both groups.

To present day, there is no consensus among clinicians on the indications for surgical intervention in IMR. The question of choosing between annular reduction alone or combining it with the correction of severe structural changes in the valve, as well as whether to perform mitral valve repair or replacement in IMR, remains under discussion [5]. Chemtob RA, et al, confirmed that mitral valve repair is more appropriate than replacement in IMR [4]. Others argue that neither repair nor replacement directly addresses the pathophysiological issues caused by IMR and that replacement is a more reliable option. That is, current recommendations do not clearly indicate whether mitral valve repair or replacement should be preferred in the correction of IMR. It is noted, however, that the frequency of recurrent mitral regurgitation is reduced after valve replacement [8]. Others believe that ischemic mitral regurgitation is not solely a disease of the annulus and that isolated annuloplasty cannot substitute for valve replacement. On the other hand, valve implantation (especially mechanical valves) requires lifelong anticoagulation therapy and does not support possible ventricular remodeling in the postoperative period [13]. Nappi F. and colleagues state that functional mitral regurgitation is one of the most common complications in adults after myocardial infarction, posing significant clinical and economic burdens [10]. Despite controlled randomized trials, many questions regarding its treatment remain unanswered [15]. The outcomes of surgical correction of IMR are still complicated by a high recurrence rate of regurgitation and the need for reoperation. Therefore, investigations into the main mechanisms of repair failure continue, as do discussions about indications, optimal timing, and the most suitable surgical technique [3]. In short, literature analysis shows that there is still no unified opinion on the exact criteria for surgery in patients with IMR.

Many preoperative echocardiographic predictors have been identified as factors that worsen prognosis in relation to recurrent ischemic mitral regurgitation (MR) and therapy failure after smaller-sized annuloplasties. These include: LV end-diastolic dimension >65 mm, mitral diastolic annulus size ≥37 mm, posterior mitral leaflet angle >45° (indicating severe restriction), anterior leaflet distal angle >25°, systolic

tenting area >2.5 cm², distance between annular plane and coaptation point >10 mm, interpapillary muscle end-systolic distance >20 mm, and systolic sphericity index >0.7 [10].

In conclusion, ischemic mitral regurgitation can be accurately diagnosed through a combination of anamnesis, clinical and instrumental evaluations, particularly transthoracic and transesophageal echocardiography, which play a key role. The developed algorithm, based on comprehensive assessments, enables optimal surgical intervention tailored to each patient, improving both short- and long-term outcomes. Surgical interventions guided by the algorithm resulted in low hospital mortality, improved quality of life, and stable results. However, the observed early postoperative mortality rate (11.36 %) and five-year survival rate (not exceeding 86.72 %) indicate that this major issue remains unresolved. Continued scientific research is needed to address emerging pathophysiological challenges in IMR.

Conclusions

1. The algorithm used for IMR treatment integrates three stages: objective-clinical signs, predictors from comprehensive evaluations, and intraoperative assessments (ad oculus+TEE).

2. If 90 % of indicators from all three algorithm scales are met, surgical treatment should be indicated. For mild cases, isolated myocardial revascularization (RV) is recommended; for moderate cases, RV+mitral valve reconstructive procedures; and for severe cases, RV+mitral valve replacement.

3. No significant difference was observed between the short- and long-term outcomes of posterior annuloplasty using the three-pledget suture method and isolated ring annuloplasty.

4. According to the algorithm: good outcomes were seen in 85.6 % of cases; satisfactory outcomes in 10.6 %; unsatisfactory outcomes in 0.76 %; mortality in 3.03 %. In the comparison group: good outcomes were 80 %; satisfactory 10.8 %; unsatisfactory 3.08 %; mortality 6.15 %. Five-year survival: 86.72 % in the main group, 83.6 % in the comparison group, and 79.31 % after mitral valve replacement (vs. 44.44 % in the comparison group).

5. An increase of 5–20 points in all quality-of-life parameters were recorded in the main group vs. 1.2–15 points in the comparison group. Comparative analysis confirmed the effectiveness of the developed algorithm.

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