Original Article

Cukurova Anestezi ve Cerrahi Bilimler Dergisi

# Impact of GLP-1 Receptor Agonist Therapy on Metabolic Parameters and Cardiovascular Risk: A Real-World Study

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**Abstract**

**Background:** Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have been shown to improve metabolic parameters and may reduce cardiovascular risk profile of individuals diagnosed with obesity and/or type 2 diabetes. This study aimed to evaluate the effects of semaglutide on anthropometric, metabolic, and cardiovascular risk parameters over three months of treatment. **Methods:** A total of 187 patients received semaglutide therapy and were assessed at baseline (0th month) and after three months (3rd month). Anthropometric measurements, laboratory parameters, and cardiovascular Score-2 were recorded. Changes were analyzed using the Wilcoxon signed-rank test, and percentage changes over the study period were calculated. **Results:** After three months, considerable declines were observed in body weight (−5.6%, $p < 0.001$), BMI (−1.9%, $p < 0.001$), systolic blood pressure (−3.5%, $p < 0.001$), diastolic blood pressure (−5.6%, $p < 0.001$), fasting blood glucose (−5.5%, $p < 0.001$), HbA1c (−7.0%, $p < 0.001$), and LDL cholesterol (−8.3%, $p < 0.001$). No significant changes were noted in ALT, AST or creatinine levels. Cardiovascular Score-2 significantly decreased from 8.8 ± 5.2 to 7.4 ± 4.7 ($p < 0.001$). Risk distribution changed markedly, reflecting an expansion of the low-risk group from 27 to 47 alongside a contraction of the high-risk group from 83 to 46. **Conclusions:** Three months of semaglutide treatment significantly improved metabolic parameters and resulted in a favorable decline in cardiovascular risk among patients. Collectively, the data point toward a beneficial cardiovascular impact of GLP-1 RAs in real-world practice.

**Keywords:** GLP-1 agonist; semaglutide; cardiovascular risk; obesity; HbA1c

## 1. Introduction

Obesity and type 2 diabetes mellitus (T2DM) are considerable global health challenges significantly associated with increased cardiovascular disease (CVD) risk[1]. These conditions frequently coexist with hypertension, dyslipidemia, and insulin resistance, contributing to a complex cardiometabolic burden. As a result, effective management strategies must extend beyond glycemic control to also target weight reduction, lipid regulation, and blood pressure optimization[2,3].

The therapeutic relevance of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) in obesity and type 2 diabetes mellitus stems from their combined influence on weight loss outcomes, appetite control, and glucose metabolism[4]. Beyond their metabolic actions, a growing body of evidence indicates that GLP-1 RAs provide clinically meaningful

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cardiovascular protection. A decreased incidence of major adverse cardiovascular events has been consistently reported in landmark studies evaluating GLP-1 RAs treatment, suggesting meaningful cardiovascular protection in high-risk individuals[5,6].

Importantly, the cardioprotective effects of GLP-1 RAs appear to extend beyond improvements in body weight and glycemic indices. Proposed mechanisms include anti-inflammatory effects, enhanced endothelial function, and modulation of lipid metabolism. Moreover, recent large-scale studies have shown that these benefits are not limited to individuals with diabetes; GLP-1 RAs have also shown beneficial cardiovascular outcomes in patients with obesity but without established diabetes, highlighting their broader therapeutic potential[7,8].

Despite the accumulating evidence linking GLP-1 RAs therapy to improved cardiovascular outcomes, relatively few studies have assessed their impact on short-term, clinically used cardiovascular risk estimation tools such as the SCORE-2 model. Understanding whether GLP-1 RAs therapy leads to measurable improvements in calculated cardiovascular risk over a short treatment window is valuable for real-world clinical decision-making[9-11].

Therefore, this research aimed to evaluate the effects of a three-month semaglutide treatment regimen on anthropometric measures, metabolic parameters, hemodynamic indices, and SCORE-2 cardiovascular risk scores among adults receiving GLP-1 RAs therapy in routine clinical practice. By integrating biochemical, clinical, and risk-score–based outcomes, this study provides a multidimensional evaluation of the early cardiometabolic effects of semaglutide.

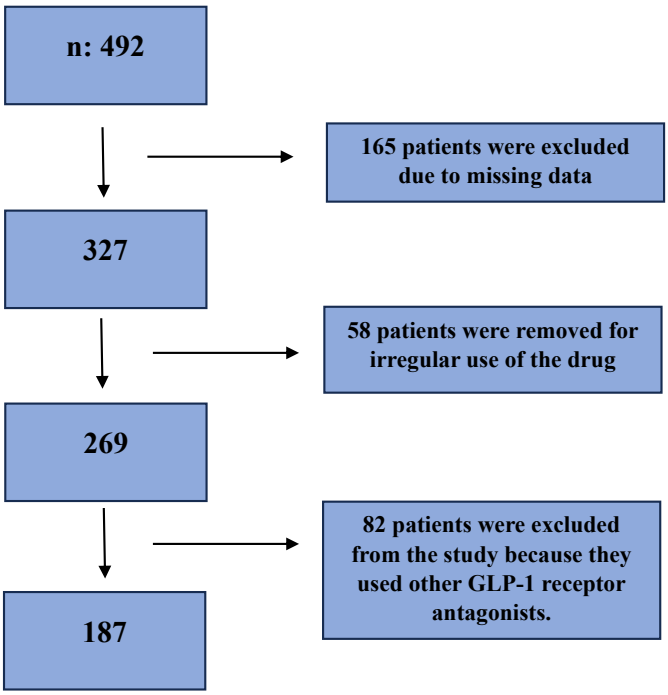


**Figure 1. Patient selection algorithm**

## 2. Methods

*2.1.Ethics Committee*

The research protocol received approval from the Institutional Review Board (01.10.2025, decision no: 2025-19/6) and was implemented in line with the ethical standards outlined in the Declaration of Helsinki. All individuals provided written informed consent before participation.

*2.2.Design and Setting of the Study*

An observational study design was employed to evaluate the effects of GLP-1 receptor agonist therapy, specifically semaglutide, on cardiovascular risk profiles, metabolic parameters, and related laboratory findings over a three-month follow-up period. Semaglutide treatment was initiated at a weekly dose of 0.25 mg during the first month and subsequently increased to 0.5 mg weekly for the remaining two months, in accordance with routine clinical practice. The study was conducted in a tertiary referral center with expertise in diabetes management and cardiovascular risk prevention.

*2.3.Study Population*

Initially, 492 patients were screened, and data were collected from 187 patients who met the inclusion criteria (Figure 1).

The study included patients using GLP-1 receptor agonists as part of their standard care and observed without intervention. Patients between the ages of 18 and 80 who had used GLP-1 RAs were included in the study.

Smoking status was documented at baseline and re-evaluated at month 3. No changes in smoking behavior were reported during follow-up; therefore, the smoking variable remained unchanged in SCORE-2 calculations.

Exclusion criteria:

- Being under 18 and over 80 years old
- Severe renal impairment (eGFR <30 mL/min/1.73 $m^2$) and dialysis patients
- Patients who changed the dose and frequency of their medication
- Pregnant and lactating patients
- Patients with active malignancies
- Patients with irregular treatment, medication changes, or missing data during follow-up
- Patients with liver failure
- Patients whose hypertension or hyperlipidemia treatment changed during follow-up to avoid affecting cardiovascular score results
- Patients taking herbal products or supplements

*2.4.Data Collection*

At study entry (month 0), participants' demographic profiles, clinical variables, and laboratory parameters were systematically documented concurrent with the initiation of GLP-1 receptor agonist therapy. Follow-up assessments were conducted at the third month following treatment initiation. The primary variables evaluated included body weight, body mass index (BMI), systolic and diastolic blood pressure (SBP and DBP), fasting blood glucose (FBG), glycated hemoglobin (HbA1c), lipid parameters (triglycerides, low-density lipoprotein [LDL]), renal function indicator (creatinine), and hepatic enzymes (aspartate aminotransferase [AST] and alanine aminotransferase [ALT]). Cardiovascular risk was estimated using the SCORE-2 risk assessment model. All clinical and biochemical measurements were obtained in accordance with standardized clinical and laboratory procedures.

*2.5.SCORE-2 Risk Assessment*

To determine the 10-year cardiovascular risk, the SCORE-2 risk assessment tool was employed, taking into account demographic and clinical variables such as age, sex, smoking status, systolic blood pressure, and lipid profile components. The European Society of Cardiology's SCORE-2 calculation system was used as a basis. For participants with diabetes, the model incorporates additional corrections to improve risk prediction accuracy. Patients were categorized as low (<5%), moderate (5–10%), or high (≥10%) risk in accordance with SCORE-2 thresholds. Given the age-optimized structure of the SCORE-2

system, risk assessments were performed at baseline (month 0) and repeated at month 3 to evaluate the impact of GLP-1 RAs treatment.

*2.6.Intervention*

Patients received GLP-1 RAs as part of their obesity regimen. No other changes to their baseline antihyperlipidemic or antihypertensive medications were made during the study to ensure the isolated evaluation of GLP-1 RAs effects. Patients requiring additional medical interventions during follow-up were excluded.

*2.7.Outcomes*

The main outcome measure was the change in cardiovascular risk as assessed by the SCORE-2 score from baseline to three months.

*2.8.Statistical Methods*

Normality of data was examined using the Shapiro–Wilk test. Normally distributed continuous variables were reported as mean ± standard deviation, while non-normally distributed data were expressed as median (minimum–maximum). Categorical variables were presented as frequencies and percentages. Given that the study included two repeated measurements (baseline and 3rd month), paired comparisons were conducted. For normally distributed variables, the paired samples t-test was used, while the Wilcoxon signed-rank test was applied for variables that did not meet normality assumptions. Statistical significance was defined as a two-sided p value < 0.05. Data analysis was carried out with SPSS version 26.0 (IBM Corp., Armonk, NY, USA).

## 3. Results

A total of 187 patients were included in the study. Anthropometric and laboratory parameters before and after three months of semaglutide treatment are summarized in Table 1. Significant reductions were observed in body weight (mean ± SD: 86.7 ± 11.6 kg vs. 81.8 ± 11.1 kg, $p < 0.001$), body mass index (BMI) (31.5 ± 4.5 kg/m² vs. 30.9 ± 4.4 kg/m², $p < 0.001$), systolic blood pressure (131.1 ± 8.0 mmHg vs. 126.4 ± 6.7 mmHg, $p < 0.001$), diastolic blood pressure (81.7 ± 6.3 mmHg vs. 77.1 ± 6.2 mmHg, $p < 0.001$), fasting blood glucose (100.1 ± 10.8 mg/dL vs. 94.5 ± 9.1 mg/dL, $p < 0.001$), HbA1c (5.7 ± 0.3% vs. 5.3 ± 0.25%, $p < 0.001$), and LDL cholesterol (126.2 ± 28.9 mg/dL vs. 115.7 ± 22.6 mg/dL, $p < 0.001$) after three months of treatment. No significant changes were detected in ALT, AST or creatinine levels ($p > 0.05$ for all). Cardiovascular Score-2 significantly decreased from 8.8 ± 5.2 to 7.4 ± 4.7 ($p < 0.001$).

**Table 1. Changes in anthropometric and laboratory parameters before and after treatment (Semaglutide)**

| | 0th month | | 3rd month | | p |
|---|---|---|---|---|---|
| | **Mean ± SD** | **Median (Min-Max)** | **Mean ± SD** | **Median (Min-Max)** | |
| Weight (kg) | 86.7±11.6 | 86 (63-114) | 81.8±11.1 | 80 (60-105) | <0.001 |
| BMI, kg/m² | 31.5±4.5 | 31.2 (23.2-46.7) | 30.9±4.4 | 30.4 (22.8-45.4) | <0.001 |
| Systolic blood pressure, mmHg | 131.1±8.0 | 130 (110-155) | 126.4±6.7 | 125 (110-145) | <0.001 |
| Diastolic blood pressure, mmHg | 81.7±6.3 | 80 (60-95) | 77.1±6.2 | 80 (60-93) | <0.001 |
| FBG, mg/dL | 100.1±10.8 | 101 (77-123) | 94.5±9.1 | 95 (74-118) | <0.001 |
| HbA1c % | 5.7±0.3 | 5.8 (5.1-6.4) | 5.3±0.25 | 5.4 (4.7-6.2) | <0.001 |
| ALT (U/L) | 33.7±6.8 | 34.0 (14-45) | 34±5.9 | 35.0 (15-44) | 0.327 |
| AST (U/L) | 34.9±10.3 | 35 (4-59) | 34.6±7.9 | 35.0 (15-51) | 0.130 |
| Creatinine, mg/dL | 0.87±0.13 | 0.83 (0.57-1.24) | 0.87±0.12 | 0.90 (0.60-1.22) | 0.102 |
| LDL, mg/dL | 126.2±28.9 | 131 (49-191) | 115.7±22.6 | 116 (61-168) | <0.001 |

| | | | | | |
|---|---|---|---|---|---|
| TG, mg/dL | 175.07±57.7 | 166 (82-367) | 159.7±47.9 | 154 (78-340) | <0.001 |
| Score-2 | 8.8±5.2 | 7.8 (0.8-29) | 7.4±4.7 | 6.4 (0.90-25) | <0.001 |

*Wilcoxon test. FBG: fasting blood glucose, LDL: low-density lipoprotein, TG: triglyceride, ALT: alanine aminotransferase, AST: aspartate aminotransferase, BMI: body mass index.*

Table 2 presents the percentage changes of the parameters over the three-month period. The greatest reductions were observed in LDL (−8.3%), fasting blood glucose (−5.5%), and body weight (−5.6%). Minor changes were noted in ALT (+0.8%), and creatinine (0%).

Changes in cardiovascular risk categories are shown in Table 3. The number of patients classified as low-risk increased from 27 to 47, whereas the high-risk group decreased from 83 to 46 over three months of semaglutide therapy. The moderate-risk category showed a slight increase from 77 to 94 patients (Figure 2). These findings indicate a favorable shift in cardiovascular risk profiles following GLP-1 agonist treatment.

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**Table 2. Demographic and laboratory values transition within the three months (%)**

| | **3rd − 0th** |
|---|---|
| Weight, kg, Δ (%) | −5.6 |
| BMI, kg/m², Δ (%) | −1.9 |
| SBP, mmHg, Δ (%) | −3.59 |
| DBP, mmHg, Δ (%) | −5.63 |
| HbA1c, %, Δ (%) | −7.02 |
| FBG, mg/dL, Δ (%) | −5.59 |
| Creatinine, mg/dL, Δ (%) | NS |
| AST, IU/L, Δ (%) | −0.86 |
| ALT, IU/L, Δ (%) | 0.89 |
| LDL, mg/dL, Δ (%) | −8.32 |
| Score-2 | −15.91 |

*BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, FBG: fasting blood glucose, AST: aspartate transaminase, ALT: alanine transaminase, LDL: low-density lipoprotein, NS: non-significant.*

**Table 3. Cardiovascular risk transitions within three months**

| | **0th** | **3rd** |
|---|---|---|
| Low risk | 27 (14.4%) | 47 (25.1%) |
| Moderate risk | 77 (41.2%) | 94 (50.3%) |
| High risk | 83 (44.4%) | 46 (24.6%) |

## 4. Discussion

In this observational study of 187 patients treated with a GLP-1 receptor agonist (semaglutide) over a three-month period, we observed statistically significant and clinically relevant improvements in anthropometric, hemodynamic, glycemic, lipid, and cardiovascular risk score parameters. Specifically, mean body weight decreased by 5.6%, BMI declined, blood pressure fell, fasting glucose and HbA1c improved, LDL cholesterol decreased by ~8.3%, and the calculated 10-year risk (as per SCORE-2) decreased significantly. Furthermore, the proportion of patients classified as "low risk" increased, while "high-risk" patients decreased substantially after 3 months of therapy. These favorable shifts provide real-world evidence that semaglutide not only impacts metabolic control but may also meaningfully reduce cardiovascular risk over a relatively short period.

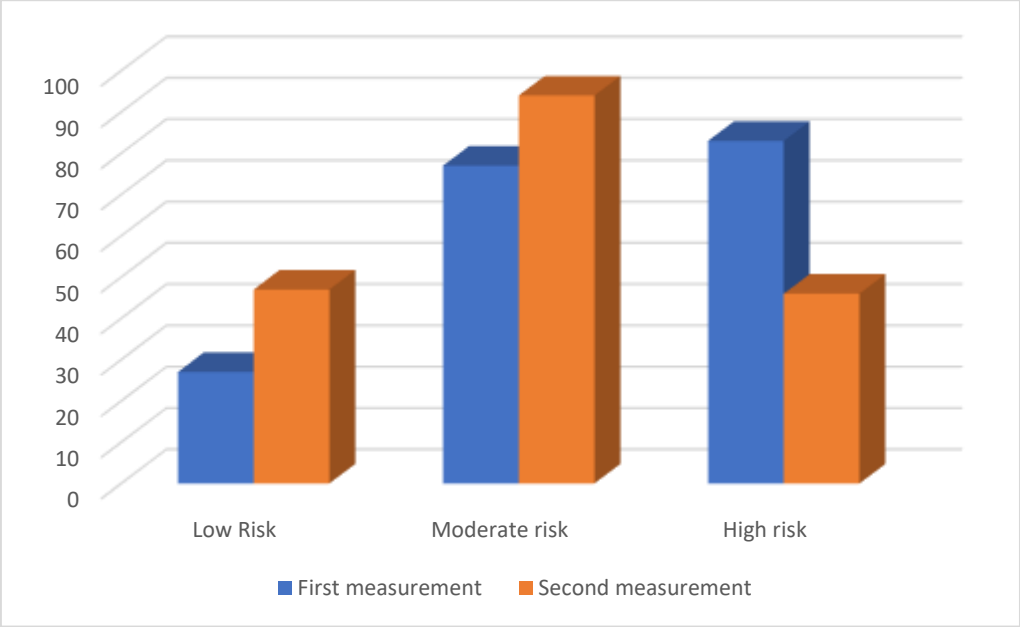


**Figure 2. Changes in cardiovascular risk category distribution at 0th and 3rd month.**

A review of the literature has shown that GLP-1 RAs improve anthropometric measurements[12]. Verma et al.'s study included 1,145 patients and found a 9.6% weight loss following semaglutide treatment[13]. Similarly, Butler et al.'s study found an 8.4% weight loss following semaglutide treatment[14]. Our study results were similar to the literature, and there was significant weight loss in our patients (5.6%).

The present findings support accumulating evidence that highlights the cardiometabolic benefits associated with the use of GLP-1 RAs. In a recent meta-analysis, GLP-1 RAs therapy in obese adults without diabetes was associated with a 19% lower risk of overall cardiovascular events, MACE, myocardial infarction, and all-cause mortality relative to placebo[15]. In the study by Shah et al., patients using semaglutide were examined and as a result of the study, a significant decrease was found in both inflammatory markers and pro BNP values[16].

Furthermore, studies have shown a reduction in cardiovascular death or MACE rates in patients using GLP-1 RAs, as well as improvements in KCCQ-CSS (Kansas City Cardiomyopathy Questionnaire Clinical Summary Score) scores[17]. In addition to these benefits, studies have also found improvements in left atrial diameter and left ventricular wall thickness in patients using GLP-1 RAs[18,19].

Evidence from controlled studies indicates that treatment strategies based on GLP-1 RAs are associated with significant reductions in overall cardiovascular events, MACE, MI, and all-cause mortality. A review of the literature found that semaglutide in the SELECT study demonstrated a reduction in primary cardiovascular events, MACE, MI, and all-cause mortality[20-22]. The Kristensen study examined seven studies from 27 publications, each involving 56,004 participants using GLP-1 RAs. Overall, GLP-1 receptor agonist therapy reduced MACE by 12%. GLP-1 RAs therapy declined all-cause mortality by 12% and heart failure hospitalizations by 9%[23].

However, most of these data come from studies with hard cardiovascular endpoints (e.g., cardiovascular death, nonfatal MI, stroke) over longer durations. What distinguishes our study is the use of a risk-scoring tool (SCORE-2) and the demonstration that meaningful risk reduction can be captured even at three months, a timeframe relevant for clinical practice and therapeutic decision-making.

Our study results not only included a reduction in cardiovascular risk, but also showed a notable enhancement of metabolic parameters such as systolic and diastolic blood pressure, HbA1c and lipid panel in patients who received treatment during follow-up. Similar to our study results, meta-analyses and studies found that GLP-1 RAs treatment was associated with significant improvements in blood pressure, lipid profile, and other cardiometabolic parameters[24-26]. According to the study by Lund et al., a decrease in blood pressure parameters, fasting blood sugar and HbA1c values was found in patients using GLP-1 RAs[27]. According to the study results, patients using GLP-1 RAs showed improvements in lipid parameters as well as weight loss and HbA1c values[28-30].

*4.1.Implications of SCORE-2 Risk Reduction*

The significant decrease in the calculated SCORE-2 score over just three months suggests that GLP-1 RAs therapy may rapidly modify an individual's cardiovascular risk profile. This is especially relevant in real-world clinical settings, where short- to medium-term therapy adjustments often precede long-term outcome data. A shift from high or moderate to lower risk categories may influence clinical decisions regarding additional preventive strategies (e.g., initiation or intensification of statins, antihypertensives, lifestyle interventions), patient motivation, and long-term management planning.

Moreover, demonstrating SCORE-2 improvement provides an argument for considering GLP-1 RAs therapy not only for glycemic control or weight loss but as part of a comprehensive cardiovascular risk reduction strategy in obesity and T2DM care.

*4.2.Strengths and Potential Limitations*

The robustness of this study is supported by its relatively large sample size (n = 187) and real-world design under routine clinical practice conditions. The use of a validated and widely used cardiovascular risk tool (SCORE-2) adds clinical relevance beyond surrogate metabolic endpoints. The consistent protocol (no changes in antihypertensive or lipid-lowering therapy) helps isolate the effects of GLP-1 RAs therapy.

However, several limitations must be acknowledged. First, the observational design lacks a comparator (placebo or non-GLP-1 RA) group, which limits causal inference. Second, the follow-up duration is relatively short (three months), and while early changes are encouraging, whether these translate into long-term reductions in hard cardiovascular events remains speculative. Third, SCORE-2—though useful—predicts risk based on population data; it does not guarantee actual reductions in events. In addition, potential confounding factors such as dietary habits, physical activity levels, and lifestyle modifications were not systematically assessed or controlled during the study period. Furthermore, lifestyle-related factors such as dietary intake, physical activity, and adherence to behavioral recommendations were not objectively measured during follow-up. Therefore, their potential contribution to the observed cardiometabolic improvements cannot be completely excluded. Finally, we did not systematically assess inflammatory markers (e.g., CRP), endothelial function, or adipokines, which might have shed light on mechanistic pathways.

## 5. Conclusion

Overall, our study provides real-world evidence that three months of semaglutide therapy can significantly improve a broad spectrum of cardiometabolic parameters and reduce estimated cardiovascular risk, as assessed by SCORE-2. These findings align with the growing literature supporting the cardiovascular benefits of GLP-1 RAs and underscore their potential role not only in glycemic and weight management, but as a component of comprehensive cardiovascular risk reduction strategies. While longer-term data with hard cardiovascular endpoints are needed, the observed early improvements are encouraging and support the use of GLP-1 RAs in clinical settings where rapid risk factor modification is desirable.

**genAI:** Artificial intelligence-assisted technology was used exclusively for language editing and grammatical refinement of the manuscript.

**Statement of Ethics:** The study was approved by the Institutional Review Board of the participating center (Approval Date: August 06, 2025; Decision No: 2025-14/17) and conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrollment.

**Data Availability:** The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

**Author Contributions:** Concept – N.Y.; Design – N.Y.; Supervision – N.Y.; Resource – N.Y.; Materials – N.Y.; Data Collection and/or Processing – N.Y.; Analysis and/or Interpretation – N.Y.; Literature Review – N.Y.; Writing – N.Y.; Critical Review – N.Y.

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**Conflict of Interest:** The authors have no conflicts of interest to declare.

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