



Perioperative Management in Patients with Diabetes Mellitus: A Comprehensive Review

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ABSTRACT

Introduction: The global prevalence of Diabetes Mellitus (DM) is rising, proportionately increasing the number of diabetic patients requiring surgical interventions. Surgery induces a profound metabolic stress response that disrupts glucose homeostasis, leading to hyperglycemia, increased insulin resistance, and a higher propensity for perioperative complications such as surgical site infections (SSI), acute kidney injury, cardiovascular events, and increased mortality. This review highlights the critical purpose of standardizing perioperative management in diabetic patients to optimize metabolic control and improve surgical outcomes.

Methods: A comprehensive narrative literature review was conducted evaluating guidelines and evidence from prominent medical societies, including the American Diabetes Association (ADA), the Indonesian Society of Endocrinology (PERKENI), and recent clinical trials. The evaluation encompasses pre-operative risk assessment, intra-operative glycemic targets, specific management of various anti-diabetic agents, and post-operative care transitions.

Results: Pre-operative management mandates a thorough risk assessment and achieving a target HbA1c of less than 8% for elective surgeries, alongside careful cessation or adjustment of oral anti-diabetic drugs, particularly emphasizing the withholding of SGLT2 inhibitors and GLP-1 receptor agonists due to specific perioperative risks. Intra-operatively, blood glucose should be maintained between 140–180 mg/dL. Tight glycemic control (80–110 mg/dL) is heavily discouraged due to the risk of undetected severe hypoglycemia. Continuous intravenous insulin infusion is recommended for major or prolonged surgeries. Post-operatively, a structured transition from intravenous to subcutaneous basal-bolus insulin is crucial once the patient achieves hemodynamic stability and resumes oral intake, avoiding the outdated sliding-scale insulin regimens.

Conclusions: Perioperative management of DM demands a highly coordinated, multidisciplinary approach involving surgeons, anesthesiologists, and endocrinologists. The implementation of individualized, evidence-based glycemic protocols across the entire perioperative continuum significantly mitigates morbidity, prevents metabolic emergencies, and improves overall patient survival and recovery.

Keywords: Diabetes Mellitus; Perioperative Care; Glycemic Control; Insulin Therapy; Surgical Outcomes; Surgical Stress.



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INTRODUCTION

Diabetes Mellitus (DM) represents one of the most significant global health challenges of the 21st century. As the prevalence of both Type 1 and Type 2 DM continues to escalate worldwide, a parallel increase is observed in the proportion of diabetic patients undergoing surgical procedures. It is estimated that up to 25% of all diabetic patients will require some form of surgical intervention during their lifetime [1]. Furthermore, patients with diabetes constitute approximately 15% to 20% of all surgical populations in tertiary care hospitals [2]. The intersection of diabetes and surgery presents a complex clinical scenario, primarily due to the intricate metabolic disturbances triggered by surgical stress and the pre-existing pathophysiological alterations inherent to the diabetic state.

Surgical trauma initiates a profound and complex neuroendocrine stress response. This response is characterized by the hypersecretion of counter-regulatory hormones, notably cortisol, catecholamines (epinephrine and norepinephrine), glucagon, and growth hormone. Simultaneously, tissue injury triggers the release of pro-inflammatory cytokines, including Interleukin-6 (IL-6), Interleukin-1 (IL-1), and Tumor Necrosis Factor-alpha (TNF- α) [3,4]. These hormonal and immunological shifts act synergistically to induce a state of severe peripheral insulin resistance, predominantly in skeletal muscle and adipose tissue, while simultaneously upregulating hepatic gluconeogenesis and glycogenolysis [5]. In a patient with pre-existing diabetes—who already suffers from either absolute insulin deficiency or established insulin resistance—this surgical stress response invariably precipitates severe perioperative hyperglycemia, lipolysis, and protein catabolism [6].

The clinical consequences of unmanaged perioperative hyperglycemia are extensively documented and severely detrimental. Elevated blood glucose levels impair critical immune functions, specifically neutrophil chemotaxis, phagocytosis, and the generation of reactive oxygen species required for bactericidal activity, thereby drastically increasing the risk of Surgical Site Infections (SSI) [7]. Additionally, hyperglycemia induces endothelial dysfunction, oxidative stress, and a pro-thrombotic state, which culminate in impaired wound healing and an increased incidence of major adverse cardiovascular events (MACE), acute kidney injury (AKI), and longer hospital stays [8]. Conversely, overly aggressive glycemic control aiming for strict normoglycemia has been shown to increase the incidence of severe hypoglycemia, which is particularly dangerous in the anesthetized patient where neuroglycopenic symptoms are masked, leading to irreversible neurological damage or fatal arrhythmias [9].

Therefore, the fundamental goal of perioperative management in diabetic patients is to navigate this delicate balance: mitigating the deleterious effects of hyperglycemia while stringently avoiding hypoglycemia and metabolic emergencies such as Diabetic Ketoacidosis (DKA) or Hyperosmolar Hyperglycemic State (HHS) [10]. This requires a highly systematic, evidence-based approach that spans the entire perioperative continuum—from the initial pre-operative evaluation in the outpatient clinic to intra-operative metabolic control in the operating theater, and finally to post-operative recovery and discharge planning.

This comprehensive review aims to synthesize the most current evidence, international guidelines—such as those from the American Diabetes Association (ADA)—and national consensus guidelines from the Indonesian Society of Endocrinology (PERKENI), to provide a robust, detailed framework for the perioperative management of patients with DM.

METHODS

This article is structured as a comprehensive narrative literature review. A rigorous search of major medical databases, including PubMed, MEDLINE, Cochrane Library, and Google Scholar, was conducted to identify relevant literature published up to the current year. Search terms included combinations of "Diabetes Mellitus", "perioperative care", "glycemic control", "surgical stress", "intraoperative insulin", and "postoperative complications". Furthermore, we extensively reviewed and synthesized current clinical practice guidelines and consensus statements from major authoritative bodies, including the American Diabetes Association (ADA) Standards of Medical Care in Diabetes, the American Association of Clinical Endocrinologists (AACE), the Society for Ambulatory Anesthesia (SAMBA), the Centre for Perioperative Care (CPOC) UK, and the Indonesian Society of Endocrinology (PERKENI). The review focuses primarily on the pathophysiological impact of surgical stress on glucose metabolism, pre-operative risk stratification, the specific pharmacological management of novel oral anti-diabetic drugs (OADs), and evidence-based protocols for insulin therapy across the pre-operative, intra-operative, and post-operative phases.

RESULTS AND DISCUSSION

The management of surgical patients with DM cannot be generalized; it must be highly individualized. It depends heavily on the specific type of diabetes (Type 1 vs. Type 2), the nature and urgency of the surgical procedure (elective vs. emergency, major vs. minor, open vs. laparoscopic), and the patient's baseline metabolic control and end-organ complications. For clarity and clinical applicability, the findings and standard of care are categorized into three distinct, chronological phases: Pre-operative, Intra-operative, and Post-operative management.

3.1. Pre-operative Management and Evaluation

The pre-operative phase is arguably the most critical period for risk mitigation. The primary objective is to evaluate the patient's overall health status, assess the adequacy of long-term glycemic control, identify diabetes-related microvascular and macrovascular complications, and formulate a tailored perioperative medication plan.

3.1.1. Pre-operative Risk Assessment and Glycemic Targets

A comprehensive history and physical examination are mandatory. Special attention must be given to cardiovascular status (ischemic heart disease, heart failure), renal function (diabetic nephropathy), and the presence of autonomic neuropathy. Cardiovascular autonomic neuropathy is of particular concern to anesthesiologists as it can manifest as resting tachycardia, orthostatic hypotension, and an increased risk of silent myocardial ischemia and profound intraoperative hemodynamic instability [11].

For elective surgeries, assessing long-term glycemic control via Hemoglobin A1c (HbA1c) is a universal standard. Current guidelines, including those from the ADA and PERKENI, strongly recommend obtaining an HbA1c level within 3 months prior to elective surgery. The universally accepted target is an HbA1c of $< 8.0\%$ (approximately corresponding to an estimated average glucose of 183 mg/dL) [12,13]. Studies consistently demonstrate that an HbA1c $> 8.0\%$ is an independent predictor of adverse surgical outcomes, particularly surgical site infections, delayed wound healing, and prolonged length of stay. For patients undergoing highly specialized elective procedures where infection carries catastrophic consequences (e.g., orthopedic joint replacements, cardiothoracic surgery), an even stricter target of $< 7.0\%$ or 7.5% may be advocated by some surgical societies, provided it can be achieved without causing significant hypoglycemia [14].

If a patient presents for elective surgery with an HbA1c $> 8.5\%$ or 9.0% , a multidisciplinary discussion between the surgeon, anesthesiologist, and endocrinologist is essential. In most cases, it is highly recommended to postpone the elective procedure to allow for a period of pre-operative metabolic optimization, typically over 2 to 4 weeks, utilizing intensified insulin regimens or medication adjustments [15]. However, for emergency or urgent surgeries, the procedure must not be delayed regardless of the HbA1c level; instead, immediate stabilization with intravenous insulin protocols is prioritized.

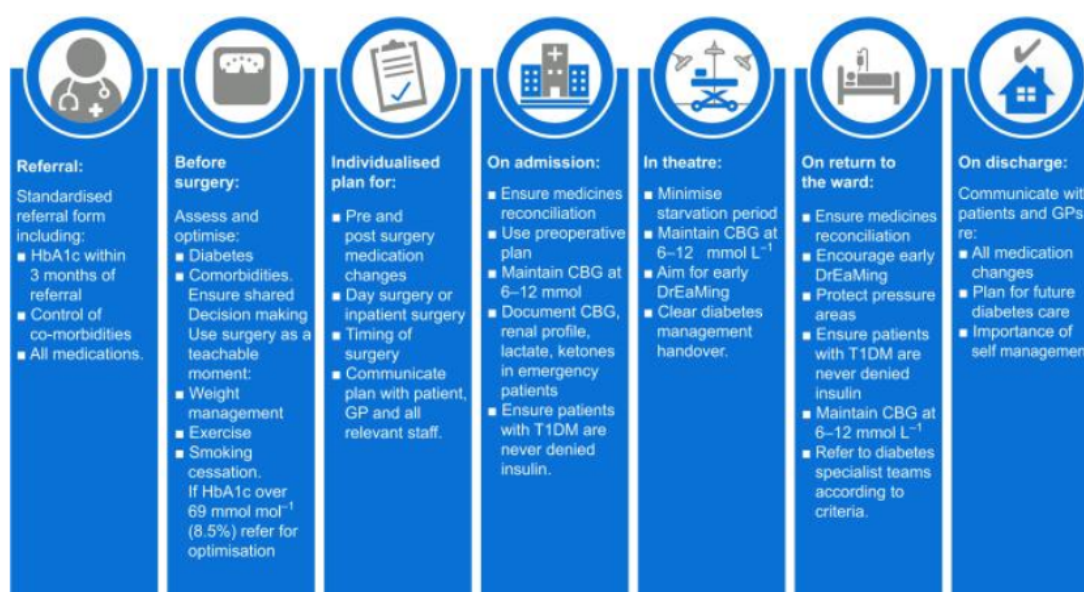


Figure 1. Algorithm for the perioperative management of DM patients

3.1.2. Management of Oral Anti-Diabetic Drugs (OADs) Prior to Surgery

The introduction of novel classes of OADs has significantly complicated pre-operative medication management. A detailed understanding of the pharmacokinetics and potential perioperative risks of each drug class is imperative.

- **Metformin:** As the first-line therapy for Type 2 DM, metformin is an insulin sensitizer that does not cause hypoglycemia. However, it carries a rare but fatal risk of Metformin-Associated Lactic Acidosis (MALA). During surgery, factors such as hypovolemia, hypoperfusion, renal impairment, and the use of iodinated contrast media can precipitate lactic acidosis. Consequently, current consensus recommends withholding metformin for at least 24 hours prior to major surgeries or any procedure requiring intravenous contrast [16]. For minor, ambulatory procedures with minimal fluid shifts, some guidelines permit continuing metformin up to the morning of surgery.
- **Sulfonylureas and Meglitinides (e.g., Glimepiride, Gliclazide, Repaglinide):** These are insulin secretagogues. Because the patient will be fasting (NPO - nil per os) prior to surgery, taking these medications poses a severe risk of profound hypoglycemia. Therefore, they must be strictly withheld on the morning of the surgery. If a patient takes a long-acting sulfonylurea the night before, careful morning glucose monitoring is required [13].
- **Sodium-Glucose Cotransporter-2 (SGLT2) Inhibitors (e.g., Empagliflozin, Dapagliflozin):** These drugs promote glycosuria and have cardiovascular and renal benefits. However, in the perioperative setting of fasting and surgical stress, they carry a significant risk of Euglycemic Diabetic Ketoacidosis (euDKA). Because blood glucose levels may remain relatively normal, this life-threatening condition is easily missed. Furthermore, their diuretic effect can exacerbate perioperative hypovolemia. The FDA and major guidelines currently mandate that SGLT2 inhibitors be discontinued at least 3 to 4 days prior to any scheduled surgery [17].
- **Glucagon-Like Peptide-1 Receptor Agonists (GLP-1 RAs) (e.g., Liraglutide, Semaglutide):** These injectable and oral agents improve glucose-dependent insulin secretion and delay gastric emptying. The delay in gastric emptying has recently raised major concerns among anesthesiologists regarding the increased risk of regurgitation and pulmonary aspiration during the induction of general anesthesia, even in patients who have adhered to standard fasting guidelines. The American Society of Anesthesiologists (ASA) currently advises withholding daily-dosed GLP-1 RAs on the day of the procedure and considering withholding weekly-dosed formulations a week prior, or utilizing point-of-care gastric ultrasound to assess gastric volume before induction [18].
- **Dipeptidyl Peptidase-4 (DPP-4) Inhibitors (e.g., Sitagliptin, Linagliptin):** These agents are generally well-tolerated, do not cause hypoglycemia, and do not significantly affect fluid balance or gastric emptying. While generally safe, standard practice usually involves withholding them on the morning of surgery, simply because the patient is NPO and not receiving enteral nutrition to stimulate the incretin effect [19].
- **Thiazolidinediones (e.g., Pioglitazone):** These insulin sensitizers can cause fluid retention and precipitate peripheral edema or heart failure. While they do not cause hypoglycemia, they are usually withheld on the morning of surgery to minimize fluid management complications during the intra-operative period [13].

3.1.3. Management of Subcutaneous Insulin Prior to Surgery

For patients on insulin therapy, the goal is to provide sufficient basal insulin to prevent DKA and uncontrolled hyperglycemia while fasting, while avoiding hypoglycemia.

- Basal Insulin (Glargine, Detemir, Degludec): Since basal insulin suppresses hepatic gluconeogenesis in the fasting state, it should never be completely stopped. Generally, it is recommended to administer 75% to 80% of the usual dose of long-acting insulin on the night before or the morning of the surgery [20].
- Intermediate-Acting Insulin (NPH): Because NPH has a pronounced peak, the risk of hypoglycemia is higher. Patients taking NPH typically take their usual dose the night before, but only 50% of the morning dose on the day of surgery [21].
- Prandial/Bolus Insulin (Regular, Aspart, Lispro): Short- or rapid-acting insulin given for meal coverage must be entirely withheld on the morning of the surgery since the patient is fasting [20].
- Continuous Subcutaneous Insulin Infusion (CSII / Insulin Pumps): For minor surgeries, pumps can often be continued at the patient's usual basal rate. However, for major surgeries exceeding 2-3 hours, or surgeries where the pump placement interferes with the surgical field or diathermy (electrocautery), the pump should be discontinued, and the patient must be transitioned to an intravenous insulin infusion [22].

3.2. Intra-operative Management

The intra-operative phase demands vigilant monitoring and dynamic intervention. The physiological stress of surgical incision and tissue manipulation causes a rapid surge in blood glucose, while anesthetics can alter glucose metabolism and mask the signs of hypoglycemia.

3.2.1. Intra-operative Glycemic Targets

Historically, the pursuit of strict normoglycemia (80–110 mg/dL) was advocated following early studies in critical care. However, landmark multi-center trials, most notably the NICE-SUGAR trial, demonstrated conclusively that intensive glycemic control significantly increased the incidence of severe hypoglycemia and was associated with higher mortality rates compared to conventional control [9].

Consequently, a paradigm shift occurred. Current guidelines from the ADA, the Society of Thoracic Surgeons, and PERKONI uniformly recommend a target blood glucose range of 140–180 mg/dL (7.8–10.0 mmol/L) for the vast majority of intra-operative and critically ill patients [12,13]. For highly selected patients, such as those undergoing cardiac surgery who are closely monitored and where infection prevention is paramount, a slightly tighter target (e.g., 110–140 mg/dL) may be acceptable, provided hypoglycemia can be absolutely avoided [23].

3.2.2. Modalities of Intra-operative Glycemic Control

The choice of insulin therapy during surgery depends on the type of diabetes, the magnitude of the surgery, and the pre-operative glycemic state.

- **Minor/Ambulatory Surgery:** For short procedures (less than 1-2 hours) in patients with well-controlled Type 2 DM, simply omitting the morning dose of OADs or utilizing the reduced subcutaneous basal insulin dose is often sufficient. Blood glucose should be checked upon arrival, intra-operatively (if the procedure extends), and in the recovery room. If glucose exceeds 180 mg/dL, subcutaneous correctional doses of rapid-acting insulin can be administered, though its absorption can be erratic under anesthesia due to skin hypoperfusion.
- **Major Surgery:** For procedures lasting more than 2 hours, surgeries involving significant fluid shifts, cardiac surgeries, and all patients with Type 1 DM, Continuous Intravenous Insulin Infusion (CIII or Insulin Drip) is the absolute standard of care [24]. Intravenous Regular insulin has a rapid onset and a very short half-life (minutes), allowing the anesthesiologist to titrate the dose minute-by-minute in response to the dynamic changes in surgical stress and blood glucose levels.

3.2.3. Intravenous Insulin and Fluid Protocols

A standardized CIII protocol is essential. The most common approach involves combining an insulin infusion (e.g., 50 units of Regular Insulin in 50 mL of normal saline, yielding 1 Unit/mL) with a separate intravenous maintenance fluid containing glucose to prevent hypoglycemia and provide basal caloric requirements.

- **Glucose substrate:** Typically, a solution of 5% Dextrose (e.g., D5W, D5-1/2NS) is infused at a steady rate of 50-100 mL/hour, delivering 2.5 to 5 grams of glucose per hour. This suppresses starvation ketosis and allows for smoother insulin titration [25].
- **Insulin titration:** The insulin infusion rate is adjusted based on hourly capillary blood glucose checks using a validated algorithmic nomogram (e.g., the Alberti regimen or modern dynamic multiplier protocols).
- **Potassium monitoring:** Because insulin drives potassium into the cells, CIII can rapidly cause hypokalemia. Serum potassium levels must be closely monitored, and potassium chloride (KCl) should be added to the maintenance fluids to maintain serum potassium between 4.0 and 5.0 mEq/L [26].
- **Non-dextrose fluids for resuscitation:** While dextrose is used for maintenance, fluid resuscitation for intra-operative hypovolemia or blood loss should utilize isotonic crystalloids without dextrose (e.g., Normal Saline or balanced crystalloids). Interestingly, Ringer's Lactate should be used with caution in diabetic patients, particularly those with hepatic impairment, as the lactate can be converted into glucose via hepatic gluconeogenesis, exacerbating hyperglycemia [27].

3.3. Post-operative Management and Transition of Care

The post-operative period is characterized by the gradual resolution of surgical stress, tissue repair, and the return to normal physiological function. Maintaining glycemic control during this phase is paramount to prevent SSI, promote collagen deposition, and facilitate early mobilization.

3.3.1. Immediate Post-operative Care in the PACU/ICU

Upon arrival at the Post-Anesthesia Care Unit (PACU) or Intensive Care Unit (ICU), the CIII must be continued until the patient is hemodynamically stable. Blood glucose monitoring should continue every 1-2 hours. In the immediate post-operative phase, hyperglycemia remains a significant risk factor for anastomotic leakage and wound dehiscence [28].

3.3.2. Transition from Intravenous to Subcutaneous Insulin

One of the most vulnerable periods in perioperative DM management is the transition from the intravenous insulin drip to subcutaneous (SC) insulin. Premature discontinuation of the IV drip without adequate SC coverage is a common medical error that rapidly leads to rebound hyperglycemia and, in Type 1 DM, diabetic ketoacidosis [29].

The transition should only occur when the patient is hemodynamically stable, off vasopressors, and has resumed reliable oral or enteral intake.

- The Overlap Rule: Because SC basal insulin takes 1 to 2 hours to begin working, the SC basal insulin must be administered 1 to 2 hours before the intravenous insulin infusion is completely stopped [12].
- Calculating the Dose: The Total Daily Dose (TDD) of SC insulin can be estimated from the IV insulin requirement. A common method is to calculate the total IV insulin used over the preceding stable 6 to 8 hours, extrapolate that to a 24-hour total, and then administer 60% to 80% of that total as the new SC TDD. This TDD is then divided into 50% basal insulin (e.g., Glargine) and 50% prandial insulin (divided across three meals) [30].

3.3.3. The Fallacy of Sliding Scale Insulin

Historically, post-operative patients were often managed using "Sliding Scale Insulin" (SSI) alone, where rapid-acting insulin is given purely reactively based on a high blood glucose reading. Extensive evidence, including the landmark RABBIT 2 Surgery trial, has unequivocally proven that sliding scale monotherapy is ineffective, results in large glycemic excursions (yo-yo effect), and increases the risk of both hyperglycemia and surgical complications [31]. The gold standard for post-operative management in the non-critical care setting is a proactive Basal-Bolus-Correction regimen. This includes basal insulin to suppress hepatic glucose output, prandial insulin to cover meals, and a small correctional scale only to fix unexpected elevations.

3.3.4. Resuming Oral Anti-Diabetic Drugs

OADs should not be rushed back into the patient's regimen immediately post-op. In the early post-operative days, surgical stress persists, and oral intake may be erratic. SC insulin remains the safest and most adjustable therapy.

OADs should only be re-instituted when the patient is eating their normal diet, gastrointestinal transit is normal (no ileus), and most importantly, renal function (creatinine/eGFR) and hemodynamic status have stabilized to pre-operative baselines [13]. Restarting metformin or SGLT2 inhibitors too early in a patient with post-operative AKI or hypovolemia can be disastrous.

3.4. Enhanced Recovery After Surgery (ERAS) in Diabetes

The implementation of ERAS pathways has revolutionized perioperative care by reducing physiological stress and accelerating recovery. However, standard ERAS protocols—which heavily emphasize pre-operative carbohydrate loading to reduce insulin resistance—require careful modification for diabetic patients.

Administering a large bolus of oral complex carbohydrates (typically 50-100 grams) 2 hours before surgery in a diabetic patient can cause profound pre-operative hyperglycemia. Current customized ERAS guidelines for diabetes suggest that clear, carbohydrate-containing drinks may be given cautiously only to patients with well-controlled Type 2 DM ($HbA1c < 7.5\%$), usually combined with specific insulin coverage. For patients with Type 1 DM, poorly controlled Type 2 DM, or gastroparesis, pre-operative carbohydrate loading is generally contraindicated due to the risk of severe hyperglycemia and delayed gastric emptying [32,33].

CONCLUSIONS

The perioperative management of patients with Diabetes Mellitus is not merely a matter of adjusting insulin doses; it represents a complex, dynamic physiological challenge that significantly dictates surgical success or failure. The detrimental cascade initiated by surgical stress and subsequent hyperglycemia necessitates a proactive, highly structured, and multidisciplinary approach involving surgeons, anesthesiologists, endocrinologists, and specialized nursing staff.

Adequate pre-operative optimization aiming for an $HbA1c < 8.0\%$, coupled with a meticulous understanding of modern anti-diabetic pharmacotherapy—particularly the perioperative risks associated with SGLT2 inhibitors and GLP-1 RAs—forms the foundation of risk mitigation. Intra-operatively, transitioning from the outdated pursuit of strict normoglycemia to a safer, evidence-based target of 140-180 mg/dL using continuous intravenous insulin infusion for major procedures has markedly improved safety profiles. Finally, the post-operative phase demands a safe, overlapped transition to subcutaneous basal-bolus insulin regimens, definitively abandoning the reactive and harmful sliding scale protocols. By integrating these standardized, evidence-based protocols tailored to the individual patient's metabolic profile, healthcare systems can drastically reduce the incidence of perioperative morbidity, minimize surgical site infections, and ensure a safer, more rapid recovery for the growing population of surgical patients with diabetes.

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