

# Management of Chronic Medication Therapies in the Perioperative Period: a Literature Review

Daniela Almeida<sup>1</sup>, Cristina Pereira<sup>1</sup>, Paula Sá Couto<sup>1</sup> and Humberto S Machado<sup>1,2,3\*</sup>

<sup>1</sup>Serviço de Anestesiologia, Centro Hospitalar Universitário do Porto, Porto, Portugal

<sup>2</sup>Instituto Ciências Biomédicas Abel Salazar, Universidade do Porto, Portugal

<sup>3</sup>Centro de Investigação Clínica em Anestesiologia, Centro Hospitalar do Porto, Porto, Portugal

\*Corresponding author: Humberto S Machado, Serviço de Anestesiologia, Centro Hospitalar Universitário do Porto, 4099-001 Porto, Portugal, Tel: +351935848475; Fax: +351 222 009483; E-mail: hjs.machado@gmail.com

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#### Abstract

**Introduction:** More than half of the patients scheduled for elective surgery are on chronic medication therapies (CMT), which make their management an essential priority for every staff member participating in the perioperative period. This review gathers information on the safest management of patients' CMT according to the most recent literature.

**Methods:** A literature review of recent expert recommendations and current evidence on management of CMT in the perioperative period was gathered by a selective search in PubMed, Medline and Embase databases was performed.

**Results and discussion:** Cardiovascular medication should generally be continued in the preoperative period, with exception of ACEIs (Angiotensin-converting-enzyme inhibitors) and ARBs (angiotensin II receptor antagonists), which increase the risks of severe hypotension under anaesthesia.  $\beta$ -blockers, if acutely withdrawn, may lead to significant morbidity and mortality. Coagulation and antiplatelet medication requires a more multidisciplinary approach, weighting ischemic risks and bleeding risks. Intravenous reversible glycoprotein inhibitors can be used as bridging therapy for patients with very high risk of stent thrombosis. Management of patients treated with New Oral Anticoagulants (NOAC) must consider both kidney function and surgical bleeding risk. Diabetic oral agents should be held prior to surgery, and substituted with insulin supplementation as required. Anti-seizure, antipsychotics and most antidepressants should be continued. Lithium should be discontinued before surgery.

**Conclusion:** The patient's comorbidities, clinical status and planned procedure must be considered when managing chronic medication in the perioperative period.

## Introduction

Over 50% of patients scheduled for elective surgery are on chronic medication therapies (CMT) [1]. This makes the recommendations regarding their management in the perioperative period one of the major priorities in anaesthetic care.

Data supporting either the maintenance or the suspension of these CMT, namely randomized controlled trials, often lack strong evidence and directive guidelines [1]. Therefore, perioperative CMT

management is largely based on the estimation of risks and potential benefits for the patient.

The objective of this review is to gather information on the safest management of CMT, based on most beneficial therapeutic endpoints regarding the patient physical status, the proposed procedure and the expected outcome. The general aspects of this review are summarized in Table 1.

	Drugs	Indications	Recommendation/evidence
	β-blockers	Continue	Class I/level B
	α2-agonists	Continue	
	ACEIs and ARBs	Discontinue 24 h before surgery	Class IIa/level C
	Diuretics	Continue	
Cardiovascular agents	Calcium channel blockers	Continue	

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		Antiarrhythmic drugs	Continue		
		Statins	Continue	Class I/level C	
		Aspirin (primary prevention)	Discontinue 7 days before surgery		
		Aspirin (secondary prevention)	Consider risks and benefits of surgery	Class IIb/level B	
		Clopidogrel	Discontinue 5 days before surgery	Class IIa/level C	
		Prasugrel	Discontinue 7 days before surgery	Class IIa/level C	
	Antiplatelet	Ticlopidin	Discontinue 5 days before surgery		
		Varfarin	Discontinue ~4 days before surgery		
		Prophylactic LMWH	Discontinue 12 h before surgery		
		Therapeutic LMWH	Discontinue 24 h before surgery		
Platelet and coagulation	Anticoagulats	New Oral Anticoagulants	*see table 2		
Endocrinology agents		Thyroid medication	Continue		
		Diabetic oral agents	Discontinue on the day of surgery		
		Insulin	Adapt dosage to needs		
		Hormonal replacement	Discontinue 1 month before surgery		
		Oral contraceptives	Continue		
		Corticosteroid therapy	Continue (may need supplementation)		
-		Irreversible MAOI	Discontinue 1-2 weeks before	surgery	
		Reversible MAOI	Discontinue on the day of surgery		
		Anti-seizure agents	Continue		
		Dopaminergic drugs	Continue		
		Antidepressants	Continue		
		Antipsychotics	Continue		
Neurological and psicoactive agents		Lithium	Discontinue one day before surgery		

 Table 1: Chronic medication management (ACEI: Angiotensin-Converting-Enzyme Inhibitors; ARB: Angiotensin II Receptor Antagonists; LMWH: Low Molecular Weight Heparin; MAOI: Monoamino Oxidase Inhibitors)

## Methods

The authors performed a literature review of existing expert recommendations and current evidence on management of CMT in the perioperative period. The evidence presented was gathered by a selective search in PubMed, Medline and Embase databases. Articles included comprised the most recent full-article and peer-reviewed publications, written in the English language. Letters and editorials were excluded. The search results were screened in a stepwise manner, beginning with selection by title, followed by selection of the content of the abstract and the full-text content.

## **Results and Discussion**

#### Chronic medication therapies

**Cardiovascular agents:** Antihypertensive medications should generally be continued preoperatively [2]. Stopping  $\beta$ -blockers or  $\alpha$ 2-agonists may be associated with rebound hypertension [3]. According to the latest guidelines from the European Society of Anaesthesiology and European Society of Cardiology (ESA/ESC), patients currently receiving  $\beta$ -blockers should continue this medication during the perioperative period (recommendation class I, level of evidence B) [4]. Their acute withdrawal may lead to significant morbidity and increased mortality [5]. In patients with clinical risk factors undergoing high-risk surgery, there is some evidence supporting a decrease in cardiac mortality and myocardial infarction with  $\beta$ -blockers therapy [6]. For this reason, the ESA/ESC recommends that pre-operative initiation of beta-blockers may be considered in patients with two clinical risk factors or ASA status 3 or more, scheduled for high-risk surgery (recommendation class IIb, level of evidence B) [4].

For Angiotensin-converting-enzyme inhibitors (ACEIs) or angiotensin II receptor antagonists (ARBs), transient discontinuation (24 h) before non-cardiac surgery should be considered when they are prescribed for hypertension, especially for patients with risk of severe hypotension under anaesthesia (recommendation class IIa, level of evidence C) [4]. Through the impairment of the compensatory activation of the renin-angiotensin system during surgery, they are associated with intraoperative hemodynamic instability. However, in stable patients with heart failure and left ventricular systolic dysfunction, continuation of ACEIs or ARBs should be considered for non-cardiac surgery.

Diuretics are frequently used in patients with hypertension or heart failure. In general, when used for hypertension, should be continued in the day of surgery and resumed orally when possible [2]. When used for heart failure, dosage increments should be considered if signs or symptoms of fluid overload are present. Dose reduction or even discontinuation of the drug should be considered in patients with hypovolaemia, hypotension or electrolyte disturbance (specially hypokalaemia and hypomagnesaemia) [4].

Calcium channel blockers are used for hypertension and vasospastic disease and should be continued in the perioperative period [4]. In the latter, withdrawal can cause severe vasospasm.

Antiarrhythmic drugs should be continued before surgery, but can usually be discontinued for a few days and resumed when the patient can take oral drugs [4]. Drugs with long duration of action such as digoxin and amiodarone can safely be discontinued and restarted when possible. If necessary, intravenous doses of either digoxin or amiodarone could be used if the fasting period is extended or if is clinically indicated.

Multiple observational studies have suggested that perioperative statin use has a beneficial effect on 30 day and long-term mortality, and cardiovascular events [7,8]. A series of observational studies suggest that perioperative statin therapy is also associated with a lower risk of acute renal failure [9]. ESA/ESC Guidelines strongly recommended peri-operative continuation of statins, favouring statins with a longer half-life or extended-release formula (recommendation class I, level of evidence C) [4].

## **Platelet and Coagulation Drugs**

#### Antiplatelet agents

Antiplatelet agents inhibit platelet aggregation, which may increase intraoperative blood loss and haemorrhagic complications. However, the same effect can help prevent perioperative vascular complications, particularly cardiac and thromboembolic events. Newer more potent antiplatelet agents have been developed, and recent reviews indicate that these newer agents offer greater efficacy and ease of administration, but are more difficult to monitor or reverse, increasing the adverse implications of residual drug levels [10].

The management principles are the same as for older agents: they require assessing the bleeding risk of the procedure and patient factors that increase such risk, as well as assessing the thrombotic risk if the agent is ceased.

Patients on aspirin for primary cardiovascular prevention may discontinue this drug seven days before surgery [4]. These patients are considered at low risk for cardiovascular events. Patients on aspirin for secondary prevention are considered at moderate to high risk for cardiovascular events, and so, should continue aspirin therapy during the perioperative period [4]. If a patient is taking aspirin for prevention of a remote medical problem and is scheduled for a surgical procedure in which the risk of perioperative haemorrhage is high and could even be catastrophic, a decision regarding the risks and benefits of discontinuing the drug before surgery must be made. Patients are often on dual anti-platelet therapy, most commonly with aspirin and a thienopyridine agent. Thienopyridine derivatives (clopidogrel, prasugrel and ticlopidin) are platelet P2Y12 receptor blockers used in patients who have had previous cerebrovascular events, recent acute coronary syndromes or percutaneous coronary interventions with stenting. They are potent antithrombotic agents that increase the risk of surgical bleeding. The management of anti-platelet therapy in patients who have undergone recent coronary stent treatment should be discussed between the surgeon, the anaesthesiologist and the cardiologist, so that the balance between the risk of life-threatening surgical bleeding and the risk of life-threatening stent thrombosis can be considered. Current guidelines from ESA/ESC recommend delaying elective non-cardiac surgery until completion of the full course of dual anti-platelet therapy and, whenever possible, performing surgery without the discontinuation of aspirin. Therefore, elective surgery should be postponed for a minimum of 4 weeks (ideally for up to 3 months) after a bare metal stent implantation, 12 months for first generation drug-eluting stent, and 6 months for new-generation drugeluting stent [4]. In patients undergoing myocardial revascularization for high-risk acute coronary syndrome, dual anti-platelet therapy is recommended for 1 year irrespective of stent type [4]. In patients in need of surgery within a few days, current ESA/ESC guidelines recommend withholding clopidogrel and ticagrelor for five days and prasugrel for seven days prior to surgery unless there is a high risk of thrombosis [4]. For patients with a very high risk of stent thrombosis, bridging therapy with intravenous reversible glycoprotein inhibitors, such as eptifibatide or tirofiban, should be considered [4]. Cangrelor, the new nonthienopyridine adenosine triphosphate analogue, is an intravenous antagonist of the P2Y12 receptor characterized by rapid, potent, predictable and reversible platelet inhibition, which should be considered for bridging patients in these situations [4].

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## **Anticogulant Agents**

Anticoagulant therapy is associated with increased risk of bleeding during surgery. Some patients with moderate to high risk of thromboembolism may require perioperative bridging with heparin (unfractionated heparin or low molecular weight heparin), whereas in patients with low risk of thrombosis, anticoagulation therapy should be stopped to minimize bleeding complications. Before making any decision about suspension of the anticoagulant therapy, all patients should be individually evaluated for the risk of thromboembolism.

In patients treated with oral anticoagulant therapy using vitamin K antagonists (VKA), it is recommended that these agents should be stopped 3 to 5 days before surgery (depending on the type of agent), until international normalized ratio (INR) measurements  $\leq 1.5$  is reached. If INR is  $\leq 1.5$ , surgery can be performed safely [4].

In patients treated with the non-VKA direct oral anticoagulants, all of which have a well-defined 'on' and 'off' action, bridging to surgery is in most cases unnecessary due to their short biological half-lives. Kidney function is essential for tailoring these agents' therapy, as well as assessment of the risk of bleeding due to the surgical procedure. Table 2 summarizes their proposed discontinuation before surgery, according to renal function and risk of bleeding. For example, patients on dabigatran therapy, submitted to surgery with low risk of bleeding should suspend dabigatran at least 48 h if the creatinine clearance (CrCl) is above 50 mL/min, and at least 60 h the CrCl is below 50 mL/ min. The same patient submitted to a surgery with high risk of bleeding, should suspend dabigatran at least 72 h if CrCl is above 50 mL/min, at least 96 h CrCl between 30 and 50 mL/min and at least 120 h if CrCl below 30 mL/min [4].

	Discontinue Before Surgery					
	Low R Bleeding	lisk of	High Risk of Bleeding			
Oral Anticoagulants	GFR ≥ 50	GFR<5 0	GFR ≥ 50	GFR 30-50	GFR<30	
Rivaroxaban	≥ 20 h	≥ 48 h	≥ 36 h	≥ 60 h		
Dabigatran	≥ 48 h	≥ 60 h	≥ 72 h	≥ 96 h	≥ 120 h	
Apixaban	≥ 36 h	≥ 48 h	≥ 60 h	≥ 72 h		

 Table 2: New Oral Anticoagulants Management (GFR: glomerular filtration rate).

Patients on rivaroxaban therapy, submitted to a surgery with low risk of bleeding should suspend rivaroxaban at least 24 h if CrCl is above 50 mL/min, and at least 48 h if CrCl is below 50 mL/min. The same patient submitted to a surgery with high risk of bleeding should suspend rivaroxaban at least 36 h if CrCl is above 50 mL/min, and at least 60 h if CrCl is below 50 mL/min [4].

Patients on apixaban therapy, submitted to a surgery with low risk of bleeding should suspend apixaban at least 36 h if CrCl is above 50 mL/min, and at least 48 h if CrCl is below 50 mL/min. The same patient submitted to a surgery with high risk of bleeding, should suspend apixaban at least 60 h if CrCl above 50 mL/min and at least 72 h if CrCl below 50 mL/min [4].

## Pulmonary Agents

This group of drugs consists primarily of those used to treat asthma and/or chronic obstructive lung disease. Patients should continue all medications through the day of surgery. Patients using inhalers can use them immediately before surgery and can resume them soon after surgery. This recommendation applies to inhaled steroids,  $\beta$ -agonists and anticholinergic agents. Patients under chronic therapy with systemic steroids (prednisolone>10 mg/day) should receive a stressdose corticosteroids supplementation [11].

Little is known about the implications of stopping leukotriene inhibitors or lipoxygenase inhibitors before surgery, which have no parenteral formulations. These agents should therefore be continued until the morning of surgery.

#### **Endocrine Agents**

Glycemic control in diabetic patients is a balance between their carbohydrate intake and use, which is greatly influenced by their corrective usage of oral medication or insulin. Although currently there is no consensual target for glucose levels, in general the literature suggests keeping them between 150 and 200 mg/dL (8 to 11 mmol/L) during the perioperative period [12].

In general, diabetic oral agents should be held on the morning of surgery, with sliding-scale insulin supplementation as needed. Metformin and thiazolidinediones act as sensitizers of specific tissues to insulin.

Metformin should be discontinued before surgery due to renal function impairment and increased risk of lactic acidosis [12,13]. As for thiazolidinediones, these are generally discontinued as they may cause fluid retention in the postoperative period [12,13]. Alpha glucosidase inhibitors act on intestinal mucous membranes, lowering the absorption of glucose after meals. However, in preoperative fasting states this drug has no effect and thus should be discontinued until the patient resumes eating [12,13]. Sulfonylureas trigger insulin production and may induce hypoglycaemia in a fasting preoperative patient, and should therefore be discontinued [13]. Glucagon-like peptide-1 (GLP-1) agonists are held the day of surgery as they slow gastric motility and may delay restoration of proper gastrointestinal function during recovery. Finally, because dipeptidyl peptidase-4 (DPP-4) inhibitors work by a glucose dependent mechanism they may be continued if necessary. However, their effects will have no important influence in preoperative fasting patients [12].

In patients using insulin, frequent glucose monitoring is needed to ensure its values are within normal ranges. In any patient who is nil per os, levels should be monitored every 4 to 6 h. Long-acting insulin given once daily should have its dose reduced in 20% on the day before surgery. If taken in the morning, decrease 20% the dose in the morning of the surgery [13]. Long-acting insulin given twice daily or biphasic insulin doesn't need any changes on the day before surgery, and on the morning of surgery the dose should be halved [13]. Short acting and intermediate-acting insulin need no changes on the day before surgery, and on the morning of surgery the total dose of morning insulin should be calculated and given only half as intermediate-acting [13].

Patients taking steroids on a long-term basis should take their usual dose on the day of surgery. Stress-associated adrenal insufficiency may occur in patients taking steroids unless additional steroid therapy is instituted perioperatively. The hypothalamic-pituitary-adrenal axis is not suppressed in patients who take less than 5 mg/day of prednisone

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or its equivalent. Generally, patients taking more than 10 mg a day need intraoperative supplementation [14]. Surgical procedures also induce a variable range of stress; thus, the amount of supplementation should vary based on the estimated amount of surgical stress and the long-term daily dose of steroid. It is important to consider that patients who took high-dosage steroid therapy maintain the risk adrenal of insufficiency for up to 1 year after the cessation [14].

Patients taking levothyroxine for hypothyroidism and patients taking propylthiouracil or methimazole for hyperthyroidism should stay on their usual dose throughout the perioperative period [15]. Because of the long half-life of the levothyroxine (seven days), it can be withheld for a few days if necessary without any untoward effect. For patients who can't tolerate oral medication for a period longer than 5 days, intravenous levothyroxine can and should be administered at a dose between 60% and 80% of the oral dose [15]. For patients with overt hyperthyroidism requiring urgent or emergent surgery, close monitoring and management of cardiac status are the main priorities. Thionamides, including propylthiouracil, methimazole and carbimazole inhibit production *de novo* of thyroid hormone but do not actually affect the release of preformed hormone. Thus, their effects may not be apparent for several days or weeks [16].

# **Hormonal Agents**

Postmenopausal hormone replacement therapies that contain oestrogen increase the risk of thromboembolic events [17]. It may therefore be reasonable to discontinue these medications before surgeries. However, they must be stopped approximately 1 month preoperatively for coagulation function to return to baseline. Most modern oral contraceptives contain low doses of oestrogen that minimally increase thromboembolic risk and, due to the risk of unanticipated pregnancy, the decision of discontinuing oral contraceptives preoperatively should be individualized [2].

# Neurological Agents

One of the most common issues for hospitalized patients with Parkinson's disease is the appropriate administration of oral medications. The inability to administer anti-parkinsonian medications properly may lead to worsening in motor symptoms and delayed recovery. However, one of the challenges for the anaesthesiology is that very few of these have an available intravenous vial, and this is problematic in patients who are unable to take oral medications for a prolonged period. Drugs for Parkinson's disease are given on a strict schedule that is unique to each patient. Planning to minimize medication interruptions will be helpful. If missing multiple doses of oral medication is unavoidable, dopaminergic agents such as subcutaneous apomorphine or transdermal rotigotine should be considered [18]. It is important to notice that these may be less tolerated or less effective than the patient's established regimens [19]. Thus, returning to a patient's home medication schedule as soon as possible should be the goal. An abrupt cessation or decrease of dopaminergic drugs (especially levodopa) can be life threatening, leading to Parkinsonism hyperpyrexia syndrome. They should be continued in the morning of surgery, as much as possible, respecting the exact schedule. If a patient is taking a monoamine oxidase-B inhibitor, such as rasagiline or selegiline, these can be continued during the perioperative periode, but drug interaction with anesthesic drugs must be taken in count. These drugs interact with opioids (especially meperidine) and indirect acting sympathomimetic [20].

Antiseizure agents should be continued in the perioperative period whenever possible. In general, routine drug level monitoring is not required preoperatively but a prolonged intensive care unit stay may require the serum drug levels to be checked before surgery, and additional doses should be given to attain desired and steady-state drug levels. Patients should be advised to take their regular medications on the morning of surgery and regular dosing should be re-established as early as practicable after surgery. If the duration of the surgical procedure exceeds the half-life of the antiseizure agents, some of them can be administered parenterally in places where intravenous forms of phenytoin, sodium valproate, and levetiracetam are available, or carbamazepine is available as a suppository. There are also important pharmacokinetic and pharmacodynamic interactions to be considered between antiseizure agents and drugs commonly used in anaesthesia. Many of the agents used in anaesthesia possess both proconvulsant and anticonvulsant properties, which could have an impact on the choice of anaesthetic.

# **Psychoactive Agents**

Psychoactive drugs can be classified as antidepressants, mood stabilizers, antipsychotics, and anxiolytics.

**Antidepressants:** Depression is effectively treated with drugs, which increase the concentration of norepinephrine and serotonin on CNS, such as tricyclic antidepressants (TCAs), serotonin re-uptake inhibitors (SSRIs) and monoamine oxidase inhibitors (MAOI's).

**Tricyclic antidepressants:** Act by preventing presynaptic re-uptake of norepinephrine and serotonin. In addition, they have anti-muscarinic, anti-histaminic and anti-alfa1-adrenergic effects. Therefore, beyond the desired therapeutic effects, TCAs cause sedation, QT prolongation, arrhythmias, postural hypotension and reduced seizure threshold. The combination of TCAs and tramadol can result in seizures and precipitate a serotonergic crisis, so this analgesic should be avoided [21]. Patients with prolonged use of TCAs are prone to hypertensive crises when sympathomimetics like ephedrine are used. Therefore, the decision of suspending this therapy must be tailored. Physicians must be aware that abrupt withdrawal of TCAs should be avoided, mainly, because of the risk of cholinergic symptoms [21]. In addition, that may precipitate a relapse of the condition for which the drug is being used.

**Serotonin re-uptake inhibitors:** have become the most commonly used drugs in the treatment of depression. The most important implication in anaesthesia is the risk of precipitating a serotonin syndrome when tramadol or meperidine are given together with an SSRI. There is also an increased risk of bleeding due to their interference with platelet function. Withdrawal of SSRIs may cause dizziness, gastrointestinal upset and a variety of psychiatric symptoms. It is recommended to continue these drugs throughout the perioperative period.

Although less frequently used these days, monoamine oxidase inhibitors are worth considering because of the severity of the interactions with commonly used drugs in anaesthesia. The most important anaesthetic consideration for patients taking MAOI's relate to the profound vasopressor effect that may be seen after administration of both indirect and direct acting sympathomimetics. The metabolism of indirect acting sympathomimetics is inhibited, resulting in the potentiation of their action. Also, meperidine can precipitate a serotonergic crisis in patients taking MAOI. Traditionally, irreversible MAOI's are stopped 2 weeks before a surgery, although abrupt withdrawal may precipitate serious psychiatric relapse. It has

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been therefore suggested that for elective surgery patients could switch from an irreversible MAOI to a reversible MAOI (such as moclobemide) to avoid a prolonged period of discontinuation [21]. In this last case, it is acceptable to preclude the drug only in the day of surgery.

**Mood stabilizers:** Lithium is used in the treatment of mania and bipolar disorders. Its mechanism is poorly understood, although it results in a reduction in the release of neurotransmitters both in the CNS and in the peripheral nervous system, causing a prolongation of depolarizing neuromuscular block and a reduction in the requirements of anaesthetic agents. In general, it is prudent to stop lithium at least 24 h before surgery [21]. Importantly, given its narrow therapeutic index and potential toxicity, NSAIDs, which reduce the excretion of lithium by the kidneys, can result in toxic plasma levels and for that should be avoided [22].

Antipsychotics: Patients with psychotic disorders have a high relapse rate when their medication is discontinued, therefore their antipsychotics agents should not be stopped during the perioperative period. They are conventionally classified as being typical or atypical. Typical antipsychotics are a class of drugs that includes prochlorperazine and chlorpromazine. Atypical antipsychotics include drugs such as quetiapine and risperidone. They act by blocking dopamine receptors in the limbic system. In addition, these drugs also block histamine, alfa1-adrenergic and cholinergic receptors, which justify their many side effects. The anaesthesiologist must use with caution or even avoid other drugs with similar adrenergic and cholinergic effects. Other than that, there are no well-established interactions between anaesthetic agents and these drugs. Atypical antipsychotics have a more favourable side-effect profile as they have a significant lower propensity to produce extra-pyramidal side effects at clinically relevant doses.

# **Key Points**

**Cardiovascular medication:** Antihypertensive and antiarrhythmic drugs should generally be continued preoperatively. An exception is for ACEIs or ARBs when there is risk of severe hypotension under anaesthesia.

Acute with drawal of  $\beta$ -blockers may lead to significant morbidity, rebound hypertension and increased mortality.

**Coagulation and antiplatelet medication:** A multidisciplinary approach and risk stratification is critical to optimizing the perioperative period.

For antiplatelet medication, the decision should be based on patient-specific ischemic risks and surgery-specific bleeding risks.

If surgery cannot be postponed, on a very high risk of stent thrombosis patient, bridging therapy with intravenous reversible glycoprotein inhibitors should be considered.

Anticoagulation therapy should be stopped to minimize bleeding complications. Patients with moderate to high risk of thromboembolism require perioperative bridging with heparin.

Management of patients treated with NOAC must be tailor made, considering kidney function and surgical bleeding risk.

**Endocrine medication:** Diabetic oral agents should be held on the morning of surgery, with sliding-scale insulin supplementation as needed.

Perioperative steroid supplementation should vary based on the estimated amount of surgical stress and the long-term daily dose of steroid.

**Neurological and psychoactive medication:** Antiseizure and antipsychotics agents should be continued during the perioperative period, as well as most of antidepressants therapy, such as TCAs and SSRIs.

To avoid psychiatric relapse, irreversible MAOI's may be switched for reversible MAOI, whose drug can be stopped only in the day of surgery.

Due to narrow the rapeutic index, lithium should be discontinued before surgery.

# Conclusion

The patient's comorbidities, clinical status and planned procedure must be considered when managing chronic medication in the perioperative period.

Recent guidelines and current evidence, considering the pharmacological drug profile, the effects of discontinuing medication on the perioperative period and potential interaction with the anesthetic drugs, were provided in this review.

## **Conflicts of Interest**

There are no conflicts of interest.

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