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Editorial

Perioperative Medication Management in Adult Cardiac Surgery: The 2017 European Association for Cardio-Thoracic Surgery Guidelines

THE MAJORITY OF patients undergoing adult cardiac surgery are taking medications that are intended to modify cardiovascular risk factors (eg, hypertension, hyperlipidemia, diabetes) or to prevent subsequent cardiovascular events. Moreover, numerous agents are used routinely intraoperatively or postoperatively for the prevention of adverse events, whereas many other agents are indicated to treat specific postoperative complications. Multiple medications, however, carry a high risk for adverse effects or increase the risk of potentially harmful drug interactions and side effects. It is important to note that clinicians must determine whether specific agents should be continued, stopped, or replaced with different agents during the perioperative period and resumed in a timely manner during recovery. Unfortunately, the evidence for some of the most widely used medications is conflicting and limited to subgroup analyses of randomized controlled trials or to observational studies. The lack of substantial evidence has led to significant variation in clinical patterns and outpatient medication strategy worldwide.[1] Although the surgeon's experience and volume undoubtedly are pivotal for the success of treatment,[2,3] numerous recent studies suggest that optimal perioperative medical therapy contributes significantly to improved either short- or long-term survival and health-related quality of life.[4-8] However, adherence to effective therapeutic strategies remains poor, even in well-controlled surgical trials, resulting in high rates of postoperative severe complications and deaths in suboptimally treated patients.[9] Despite the vital role medications play in the outcome of patients requiring cardiac surgery, there is no robust agreement among physicians or clear guidance on how to approach medication management in the perioperative period. During the last decade, consensus statements and clinical guidelines have become increasingly congruent for several topics, including antithrombotic management,[10] the prevention and management of de novo atrial fibrillation,[11] glycemic control,[12] and secondary prevention therapies after coronary artery bypass grafting (CABG).[13] These documents have been a significant step forward because health care professionals from various fields have established collaboration and uniform standards to assess available evidence in order to improve the outcome of their patients.

At the end of 2017, the European Association for Cardio-Thoracic Surgery (EACTS) released the first dedicated guidelines on perioperative medication in adult cardiac surgery.[14] This project brought together a multidisciplinary group of specialists including surgeons, anesthesiologists, cardiologists, and clinical epidemiologists in a joint task force to systematically search, review, and grade the existing body of evidence. The scope of the guidelines was to examine several major pharmacologic classes of agents involved in the prevention of acute or late adverse events. This includes antithrombotic management, prevention and treatment of atrial fibrillation, perioperative use of renin-angiotensin-aldosterone system inhibitors and beta-blockers, lipid-lowering therapies, and the prophylactic use of steroids and ulcer prevention. The 2017 EACTS guideline also considers dosing and duration of antibiotic prophylaxis, optimal glycemic control, and basic strategies of anesthesia and analgesia that may markedly influence the outcome after surgical interventions. Treatment recommendations are based on a broad range of the published evidence, including clinical trials or observational studies and, in selected topics, expert opinion. From the task force perspective, many commonly used agents in the intraoperative or early postoperative period were excluded because they have been covered comprehensively in other clinical guidelines (eg heparin/protamine management)[15] or the agents need to be covered in more details in an upcoming expert document on the treatment of surgical complications (eg, vasopressors, inotropes, calcium). The present review focuses on the main recommendations that are most likely to affect current clinical practice.

The first noteworthy recommendation relates to stopping or continuing acetylsalicylic acid (ASA) before elective CABG. The 2017 EACTS guideline recommends that ASA should be maintained until the day of surgery, except in selected patients who are at higher risk of bleeding, including those undergoing

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redo surgeries and patients with severe chronic kidney disease or hematologic disorders. EACTS recommendations are weaker (class IIA, level C) than other recently published guidelines,[15,16] including the 2018 European Society of Cardiology/EACTS guidelines on myocardial revascularization[17] because the ATACAS trial showed that preoperative ASA neither reduced thrombotic complications nor increased bleeding complications[18] and the male patients randomly assigned to receive aspirin in the ATACAS trial had a higher mortality rate.[19] Overall, the topic remains challenging and open for future research because the current recommendations are based on the meta-analysis of small randomized controlled trials with notably different inclusion criteria.[20]

In recent years, there has been tremendous growth in the number of patients with prior percutaneous coronary intervention (PCI) or unstable coronary disease referred for CABG.[21] The 2017 EACTS guideline recommends more aggressive postoperative antithrombotic regimens. In patients who have undergone recent (<1 mo) PCI, rapid initiation of dual antiplatelet therapy (DAPT) is proposed, starting in the first 48 hours of surgery irrespective of stent type, with the continuation of treatment up to 12 months based on the PRECISE-DAPT score, which becomes an unique tool for the prediction of severe bleeding.[22] A similar concept is suggested for acute coronary syndrome patients without PCI or PCI >1 month who undergo urgent surgery after life-long single antiplatelet therapy. The goal of these recommendations is to limit the recurrence of myocardial infarction and subsequently cardiac death.[23] Although bleeding is a common concern, the recently published DACAB study demonstrated that administration of DAPT even within 24 hours after elective surgery may be safe.[24]

The guidelines also offer new and much more rigorous recommendations concerning prevention and treatment of atrial fibrillation (AF).[11] The previous proposal has been changed in that either a rhythm or rate control strategy is an equally successful treatment approach in hemodynamically stable patients with de novo AF. In our opinion, the published clinical trials tend to overestimate the success rate of the rate control strategy in the real world setting.[25] It must be emphasized that a high proportion of crossovers in the patients randomly assigned to rhythm control limits the ability of studies to show the advantages of one treatment over another. Because there is significant evidence that the rhythm control strategy also may increase exercise tolerance and mental recovery after surgery,[26] clinicians also should consider other factors, such as time to discharge, when making their therapeutic decisions. Unfortunately, clinical maintenance of rhythm control did not reduce the frequency of embolic complications.[27] Therefore, curative therapy with either unfractionated or low-molecular–weight heparin should be initiated as soon as the risk of surgical bleeding is minimized, whereas oral anticoagulation is a mandatory treatment for at least 1 month when the patient is discharged with persistent postoperative AF. For many clinicians, these recommendations will require a change in clinical practice patterns and follow-up approaches.

The guidelines also provide strong recommendations concerning the use of long-acting inhibitors of the renin-angiotensin system (RAS) in the preoperative period. It is now widely recognized that RAS blockade increases the risk of anesthesia-induced hypotension, including vasoplegic syndrome refractory to catecholamine therapy. Thus, the 2017 EACTS guidelines proposed timing of the last dose of the specific agent or the switching of long-acting to short-acting RAS blockers in patients with uncontrolled hypertension. Furthermore, the guideline also recommends administration of exclusively short-acting agents to treat hypertension in the immediate postoperative period.

What also is new is that there are data now about how to approach statins in the preoperative period. The decision against the initiation of statin therapy preoperatively reflects findings from the STICS trial.[28] That study enrolled 1,922 elective patients who had sinus rhythm to receive perioperative rosuvastatin or placebo and found that statins did not reduce the risk of postoperative AF (21% *v* 20%; p = 0.72) or myocardial damage expressed by troponin I concentration (absolute risk difference 1%, 95% confidence interval −9% to 13%; p = 0.80). However, acute kidney injury was significantly more common in the rosuvastatin group than in the placebo group (25% *v* 19%; p = 0.005). The lack of benefit of statin therapy in the STICS trial has been confirmed by other studies that found an increased incidence of acute kidney injury also among patients with chronic kidney disease.[29] On the other hand, most patients referred for cardiac surgery already are taking statins, and at the moment there is no evidence that continuation or withdrawal from statin treatment before surgery can influence outcomes. Therefore, even if the new guidelines still recommend (IIaC) continuation of therapy perioperatively as it is routine today, future studies should address the best timing for statin discontinuation before cardiac surgery.

In general, the 2017 EACTS guideline on perioperative medication management recommends many other interventions that could improve patient care. The guideline provides clinicians critical evaluation of the current body of evidence, giving useful pieces of information, diagrams, and recommendations, but also recognizes directions for future investigations. Considering that today many of these interventions may not be implemented without a multidisciplinary team approach, an enormous challenge will be in the translation of these recommendations into routine clinical practice.

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