

β -adrenergic blocking drugs in the perioperative period

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Summary : During the last years increasing evidence has indicated that patients at risk for coronary artery disease may benefit from β -adrenergic blocking therapy in the perioperative setting. It has been demonstrated that even a relatively brief treatment with β -adrenergic blocking drugs decreases the incidence of perioperative myocardial ischemia. Even more important is the observation that this reduction in perioperative ischemic events ultimately results in a decrease in long term cardiac morbidity and mortality. Despite overwhelming evidence on the beneficial effects of β -adrenergic blocking in patients with coronary artery disease, many clinicians still feel some reluctance to use this type of drugs in the perioperative period. We organized a meeting to search for the major objectives that keep anesthetists from implementing prophylactic beta blocking therapy in their daily clinical practice. In this brief review we summarize the results of this meeting and discuss the current knowledge on this subject.

Key words : Beta-blocking drugs ; Myocardial ischemia ; Perioperative ischemia.

INTRODUCTION

Myocardial ischemia causes significant alterations in cardiac function and is related to the occurrence of serious untoward events such as myocardial infarction, dysrhythmias, pulmonary edema and even death (1). The perioperative period appears to present a high risk for cardiac morbidity for the surgical patient (2,3). Thus, one of the important goals in anesthetic management during this period is to anticipate the adverse effects of ischemia and to plan for an adequate preventive strategy. During the past two decades, β -blocking therapy has been demonstrated to improve acute outcomes and long-term prognosis in ischemic heart disease in non surgical patients (4-9). The use of β -blocking therapy has also been demonstrated to reduce perioperative events among high-risk patients undergoing major noncardiac and vascular surgery (10-12). Even more important is the observation that this reduction in perioperative ischemic events ultimately results in a decrease in long term

cardiac morbidity and mortality (10). More recently the beneficial effects of β -blocking therapy have also been demonstrated in patients undergoing coronary surgery (13, 14). Despite increasing evidence on the beneficial effects of β -blocking drugs in the perioperative period, many anesthesiologists still are reluctant to use β -blocking therapy perioperatively for a variety of reasons. The consequence is that, just as for cardiological practice (15), also in anesthesiological practice, β -blocking drugs are "incredibly useful, but incredibly underutilized" (16).

The reasons for which beta blockers are currently underused, are not clear. Indeed, little is known on the attitude and the knowledge of anesthesiologists with respect to perioperative β -blocking therapy. Given the importance of the subject, the *Flemish Workgroup of Cardiothoracic and Vascular Anesthesia* organized a symposium on "**the perioperative use of β -blockers**". Three speakers with substantial expertise in the field, Prof. Dr D. Poldermans (University of Rotterdam), Prof. Dr J. J. Lehot (University of Lyon), and Dr P. ten Broecke (University of Antwerp) shared their experience with the audience. The presentation was followed by an interactive voting session which aimed to get an insight in the current practice on the use of β -blocking agents in the perioperative period. This article summarizes data from the different presentations and the results of the interactive voting on the anesthesiologists' attitude towards the perioperative use of β -blocking therapy in adult surgery.

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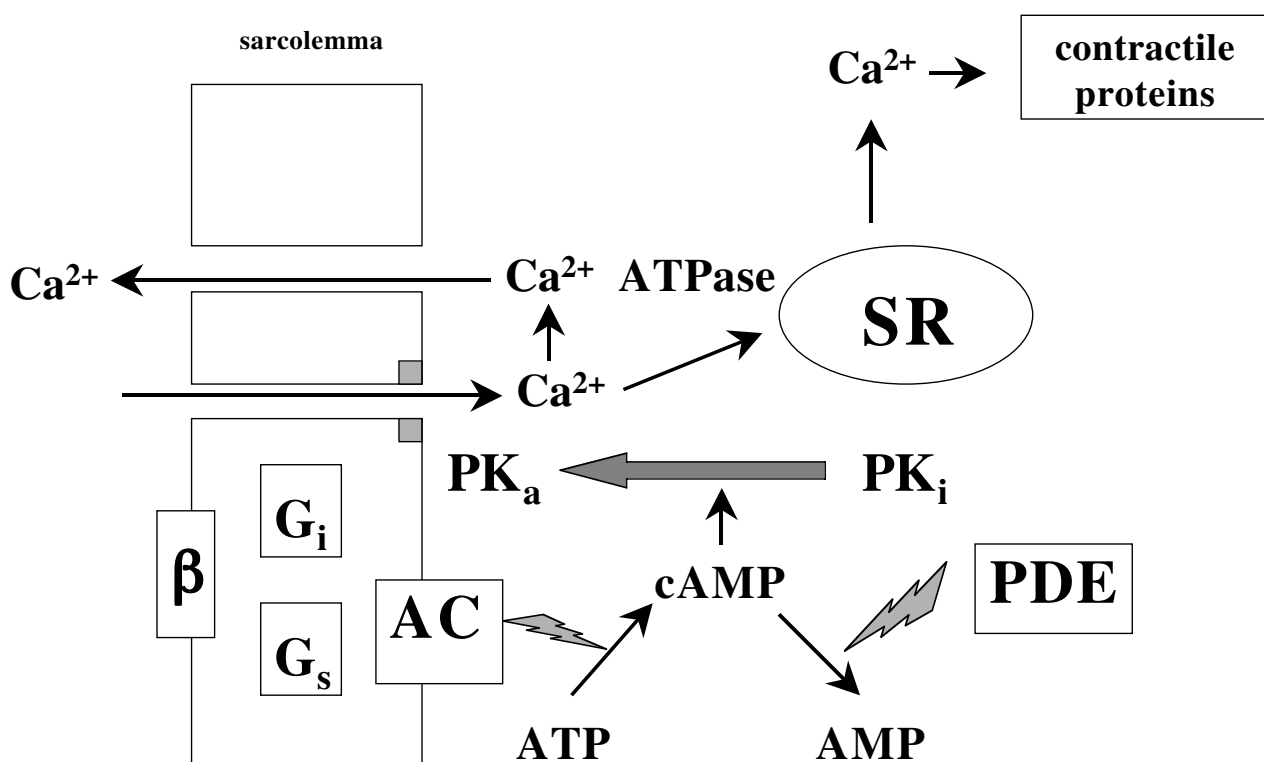


Fig. 1. — The β -receptor, adenylylase system of regulation of myocardial contraction. β = β -receptor ; G_s and G_i are the G inhibitory and the G stimulatory regulatory proteins ; AC = adenylylase ; PDE = phosphodiesterase enzyme ; PK = protein kinase (i = inactive, a = active) ; SR = sarcoplasmic reticulum.

β -RECEPTOR BLOCKADE : PHYSIOLOGY AND PHARMACOLOGY

Physiology

β -receptor physiology and pharmacology have been extensively studied (17-23). β -blocking agents exert their action by blocking the β -adrenergic receptors. β -adrenergic receptor stimulation activates a G protein which in turn stimulates adenylylase. Adenylylase (AC) converts adenosine triphosphate (ATP) to cyclic adenosine monophosphate (cAMP), which activates a protein kinase (PK). In the myocardium, this results in an opening of the voltage operated calcium channels with an influx of calcium intracellularly and an increase in contractility. Calcium is actively removed from the cytoplasm by calcium ATP-ase (Fig. 1). At least three β -adrenergic receptors have been identified. The β_1 -receptors predominate in the myocardium, the sinoatrial node, and the ventricular conduction system. Their activation increases inotropy, heart rate and conduction velocity. The β_2 -receptors are present in the smooth muscle of the blood vessels in the skin, muscle and mesentery, and in the bronchial smooth muscle. β_2 -receptor stimulation produces vasodilation and bronchial relaxation

(Table 1). The β_3 -receptors were originally thought to be involved only in the regulation of metabolic pathways but recent evidence suggests that they may also mediate a negative inotropic response (24). In addition, the existence of still a fourth subtype, β_4 has been proposed (25).

β -receptor antagonists bind competitively with the receptor. Both agonist and antagonist activity may be overruled by an increase in drug concentration. The numbers of β -receptors may decrease with chronic stimulation (down-regulation) or increase with chronic blockade (up-regulation). In congestive heart failure there is mainly a down-regulation of the β_1 -receptors (26), resulting in a relative increase in number of β_2 -receptors (27). Myocardial ischemia, on the other hand increases β -receptor density (28), although it is not clear whether this upregulation also results in a greater adrenergic response. Several studies have indeed indicated that β -receptors are shifted to a low-affinity state during ischemia (29, 30).

Pharmacology

The pharmacology of β -adrenergic blockade can be deduced from the responses elicited by the receptors in the various tissues and the activity of

Table 1
Effects of β₁- and β₂-adrenergic receptor stimulation

	β ₁ - receptor stimulation	β ₂ - receptor stimulation
cardiac		
heart rate	++	++
contractility	++	++
conduction	++	++
arterial relaxation		
coronary		++
skeletal muscle		++
pulmonary		+
abdominal		+
renal	+	+
venous relaxation		++
smooth muscle relaxation		
respiratory		+
gastrointestinal		+
urogenital		+
metabolic		
insulin secretion		+
gluconeogenesis		++
glucogenolysis		++
lipolysis	++	+
renin release	++	
cellular K ⁺ uptake		+
ADH secretion	+	

the sympathetic nerves that innervate these tissues. β-adrenergic receptor antagonists are classified as nonselective (propranolol, timolol, sotalol) and selective for β₁-receptors (cardioselective) (atenolol, metoprolol, bisoprolol, celiprololum etc.). It should be remembered that β₁ selectivity is dose dependent and is lost at higher concentrations. β-receptor antagonists are further classified as partial or pure antagonists on the basis of the presence or absence of intrinsic sympathicomimetic activity (ISA) (Table 2). Antagonists with ISA cause less myocardial depression and may therefore be better tolerated in patients with poor myocardial function. β-blockers with β₂-related ISA induce peripheral vasodilation and decrease bronchial tone. The third group of β-adrenoreceptor antagonists are those that block not only β-receptors but also α-adrenergic receptors.

CLINICAL USE OF β-RECEPTOR ANTAGONISTS

Therapeutic indications of β-adrenergic antagonists are multiple. These include treatment of hypertension and angina pectoris, suppression of cardiac arrhythmias, prevention of excessive sympathetic nervous system activity, and others. In equivalent doses, all β-antagonists appear to be equally effective in producing desired therapeutic

effects. Side effects of β-antagonists are similar for all available drugs. However, the magnitude differs depending on the selectivity and the extent of ISA. The principal side effects are related to the activity of the β-blockers on the cardiovascular and respiratory system and on the carbohydrate and fat metabolism. The principal contraindication to the administration of β-antagonists is the presence of atrioventricular heart block. Some β-blockers also possess pharmacological properties not related to adrenoreceptor activity. Carvedilol and bisoprolol have antioxidant properties (31). Carvedilol and metoprolol decrease free radical production in the neutrophils and diminish neutrophil chemotaxis (32, 33).

Perioperative use of β-blockers

Despite the initial concern that the cardiovascular effects of β-blocking agents may summate with the myocardial depressant action or vagotonic effect of anesthetic agents, β-blocking drugs have been increasingly used in the perioperative period during the last two decades. The indication was mainly *therapeutical*, aiming to control hemodynamics, cardiac dysrhythmias and myocardial ischemia associated with the stress response in the perioperative period (32-38). It is only during the last five years that significant advances have been made in defining the role of β-blockers as *prophylactic* agents in the perioperative period (39). The prophylactic property of β-blocking drugs relates to the fact that their use decreases perioperative cardiac morbidity and long term postoperative mortality.

MANGANO *et al.* (10) and WALLACE *et al.* (11) were the first to perform a randomized, double blind, placebo controlled trial on the potential effects of β-blocking therapy on perioperative cardiac morbidity and long term postoperative mortality. They demonstrated that the short term perioperative use of atenolol (starting 30 min before surgery and continued 7 days postoperatively) decreased the incidence of myocardial ischemia postoperatively by 30 – 50% and halved the long term mortality (10% in the atenolol group versus 21% in the untreated group). The effect on mortality was evident by 6-8 months and persisted to 2 years. In-hospital myocardial infarction rate however was similar in the treated and the untreated group, suggesting that the beneficial effects were mainly related to the intermediate and long term follow-up. The absence of effects of β-blocking therapy on in-hospital infarction rate was also observed in other subsequent studies (40, 41). It

Table 2
Physiological and pharmacological properties of β -adrenergic receptor antagonists

	CSA	ISA	MSA	protein binding	lipid solubility	oral bioavailability	elimination half-time	clearance	active metabolites	adult oral dose	adult IV dose
nonselective β adrenergic antagonist											
PROPRANOLOL	no	no	++	90 - 95 %	3.65	~ 25%	2 - 3 hours	hepatic	yes	40 - 320 mg/day	1 - 3 mg
NADOLOL	no	no	no	30%	0.7	~ 35%	20 - 24 hours	renal	no	40 - 160 mg/day	not available
PINDOLOL	no	++	±	40 - 60%	1.75	~ 75%	3 - 4 hours	hepatic / renal	no	10 - 40 mg/day	not available
TIMOLOL	no	±	no	10%	2.1	~ 50%	3 - 4 hours	hepatic	no	5 - 40 mg/day	not available
selective β_1 adrenergic antagonist											
METOPROLOL	yes	no	±	10%	2.15	~ 40%	3 - 4 hours	hepatic	no	50 - 400 mg/day	5 - 15 mg
atenolol tenormin	yes	no	no	5%	0.23	~ 50%	6 - 7 hours	renal	no	50 - 100 mg/day	1 - 5 mg
ACEBUTOLOL	yes	++	++	25%	1.9	~ 40%	3 - 4 hours	hepatic / renal	yes	400 - 800 mg/day	not available
ESMOLOL	yes	no	no				20 min	plasma hydrolysis		not available	1 mg/kg
BISOPROLOL	yes	no					11 hours	hepatic / renal		5 - 10 mg/day	not available
CELIPROLOLUM	yes	++	no	20 - 30%			4 - 6 hours	hepatic / renal		200 mg/day	not available
combined α and β adrenergic antagonist											
LABETALOL	no	no	±	50%		~ 20%	4 - 6 hours	hepatic	no	400 - 800 mg/day	0.1 - 0.5 mg/kg
CARVEDILOL	no	no	+				6 - 10 hours	hepatic		25 - 50 mg/day	not available

CSA = cardioselective activity ; ISA = intrinsic sympathicomimetic activity ; MSA = membrane stabilizing activity.

should be remembered that a number of criticisms have been raised with regard to the results of MANGANO and WALLACE. The most important remark concerns the fact that there was a trend towards a higher frequency of previous myocardial infarction, angina pectoris, diabetes, and advanced age in the placebo group compared to the atenolol group. In addition, there was also a trend towards a greater use of beta-blockers and angiotensin converting enzyme inhibitors at discharge in the atenolol group. It was therefore suggested that a more effective postoperative therapy in the atenolol group might have contributed to the observed outcome (39).

These first observations on the beneficial effects of the use of β -blocking agents in the perioperative period were confirmed in subsequent studies. RABY *et al.* (42) observed a significant decrease in ischemic episodes in patients in whom a target heart rate was maintained by a titrated infusion of esmolol, thereby documenting that a strict control of heart rate by β -blocking agents is indeed associated with a reduced frequency of ischemic episodes. The importance of β -blocking therapy in the perioperative period was nicely demonstrated by POLDERMANS *et al.* (43). In this prospective study, the effect of bisoprolol was evaluated in patients with documented coronary artery disease undergoing vascular surgery. In the untreated group of 53 patients, 9 patients died and another 9 patients developed a non-fatal myocardial infarction (total of 34%). In the bisoprolol group, there were only two deaths and no myocardial infarction (3.4%). This 10-fold lower mortality/morbidity incidence in the β -blocker group was highly significant ($p < 0.001$). The strong evidence for the beneficial effects of β -blocking drugs on the incidence of perioperative infarction and short term mortality, supported by this study, has led to the suggestion that in the future, perioperative care will be characterized by fewer tests, fewer coronary revascularization procedures, more use of β -blockers and fewer complications (44). The same group subsequently demonstrated that not only short-term survival was improved but that bisoprolol significantly reduced long term (2 years) cardiac death and myocardial infarction in high-risk patients after successful major vascular surgery (45).

The patients most at risk for the development of myocardial ischemic events are those with proven coronary artery disease such as patients scheduled for coronary surgery. It is interesting to note that until now little has been published on the potential beneficial effects of β -blocking therapy

on perioperative morbidity and mortality in this subset of patients. In 1999, WEIGHTMAN *et al.* (46) reported that chronic nitrate therapy appeared to be associated with increased mortality after coronary surgery and that β -blockers seemed to be associated with better survival. Only very recently, FERGUSON *et al.* (13) demonstrated a beneficial effect of preoperative β -blockade on 30-day mortality and morbidity following coronary artery surgery in North America. A similar phenomenon was recently reported for a European center (14). Another interesting finding was that in North America nearly 40% of contemporary coronary artery surgery patients were not receiving β -blocking therapy (13). A similar percentage (nearly 33%) was observed in the European study (14). It seems therefore that, despite the growing evidence on the beneficial effects of β -blocking therapy on perioperative cardiac morbidity and mortality, an important part of this patient population remains undertreated.

Underlying mechanisms of the beneficial effects of β -blocking drugs

Although the underlying mechanisms of these beneficial effects remain to be definitively elucidated, it is thought to be the result of three independent beneficial effects on the heart (39). β -blockers improve the oxygen supply-demand relationship, they have anti-arrhythmic properties, but they may also diminish the hemodynamic triggers to plaque rupture (Fig. 2). Plaque disruption does indeed play a major role in the pathogenesis of acute coronary thrombosis (47). It has been suggested that β -blockers reduce the hemodynamic forces that trigger plaque rupture, thereby decreasing the incidence of acute coronary occlusion (48).

Another possibility is that β -blockers alter the neurohumoral stress response in the intraoperative and postoperative period (39). However, to date there are no real arguments to support this hypothesis. ZAUGG *et al.* (41) observed no difference in concentrations of adrenaline, noradrenaline, cortisol and adrenocorticotrope hormone in atenolol treated patients compared with control patients. MAGUIRE *et al.* (49) reported increased levels of adrenaline and noradrenaline with intubation, despite pretreatment with the β -blocker, esmolol.

Practical implications for perioperative β -blockade : use the flow chart

The American Guidelines for Perioperative Cardiovascular Evaluation for Noncardiac

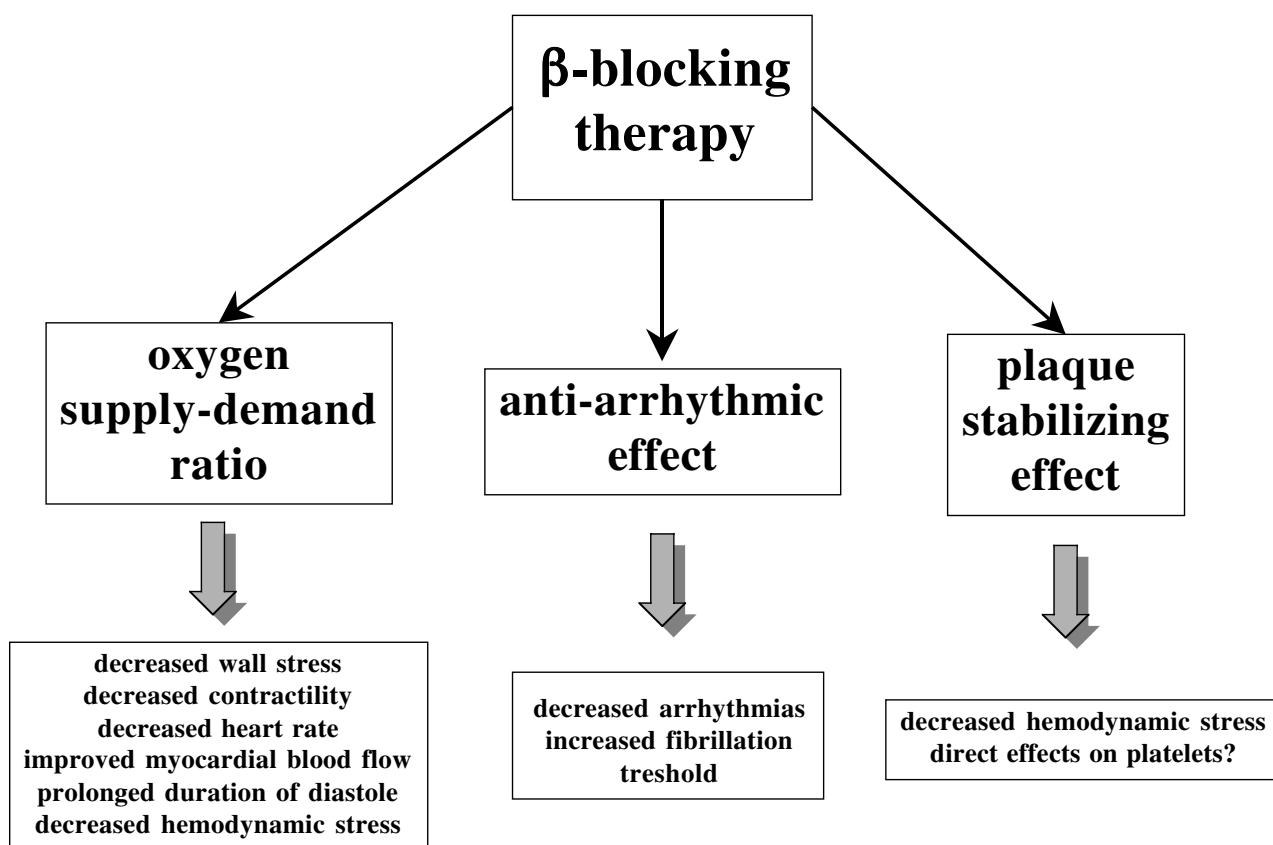


Fig. 2. — Mechanisms of the myocardial beneficial effects of β -blockers

Surgery include two classes of recommendations for the perioperative use of β -blocking drugs (50-52). Class 1 recommendations refer to the conditions in which it has unequivocally been demonstrated that β -blocking therapy is effective. These conditions include recent treatment with β -blocking drugs for angina, symptomatic rhythm disturbances, or hypertension but also the presence of preoperative myocardial ischemia in patients undergoing vascular surgery. The class 2a recommendations refer to those conditions, in which no unequivocal arguments are present but for which it is generally accepted that β -blocking therapy may be beneficial. These conditions include untreated hypertension, documented coronary disease, and risk factors for coronary disease such as age, diabetes, male sex, and vascular surgery.

How should we deal with the patient at risk scheduled for an elective intervention? A useful approach is to implement the flowchart proposed by AUERBACH and GOLDMAN (53) (Fig. 3). Based on the presence of a number of risk factors (53-55), the patients are stratified according to the degree of perioperative risk. The different risk factors are summarized in tables 3 and 4. In “high risk” patients, the incidence of cardiac complications

without perioperative β -blocking therapy is estimated to be 9 – 18% in the presence of 3 to 4 risk factors, and increases to 32% when 5 or more risk factors are present. In “intermediate risk” patients, the incidence of cardiac complications without perioperative β -blocking therapy is estimated between 2 and 6.6%, whereas in “low risk” patients, cardiac complications occur only in 0.4 – 1% of the cases. When patients are identified as “high risk”, it is advised to perform additional non-invasive cardiac evaluation (stress test) before surgery. If the patient is classified as “intermediate risk”, the global functional status of the patient should be evaluated. If coronary artery disease is suspected, or if peripheral vascular disease is present together with a poor general condition, it is also advised to perform further cardiac evaluation. If none of these risk factors are present and the patient is in good general condition, perioperative β -blocking therapy should be started and surgery can be performed.

Once the patients at risk are identified and the indication for perioperative β -blocking therapy has been defined, the therapy should be started when there are no absolute contraindications (table 5). Different possible regimens have been proposed,

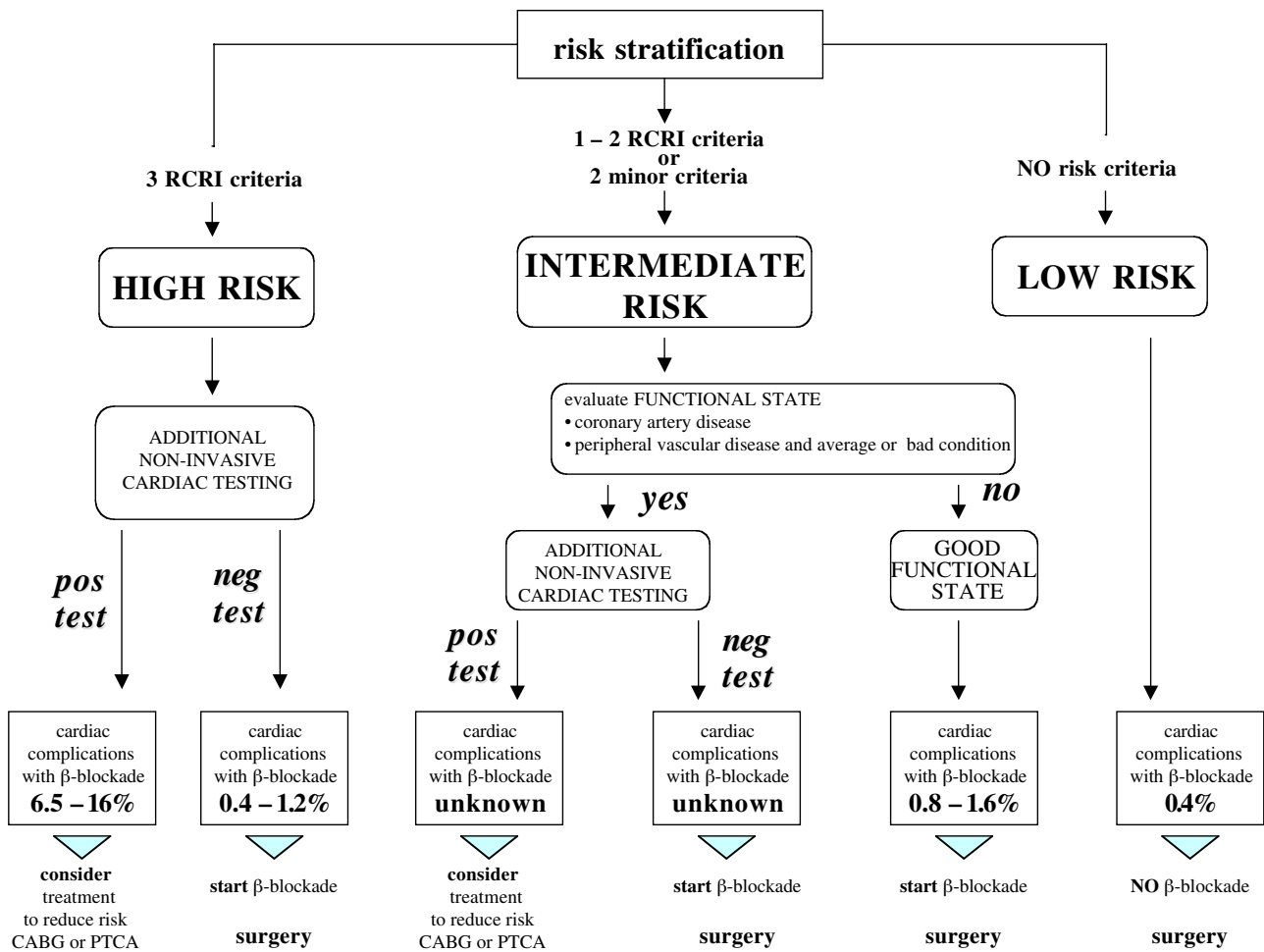


Fig. 3. — Flow chart for the administration of β-blocking therapy in the perioperative period. The minor clinical criteria are listed in Table 3 and the Revised Cardiac Risk Index (RCRI) criteria are listed in Table 4.

Table 3

Risk factors, that are indications for perioperative β-blockade, according to FLEISHER and EAGLE (ref. 54)

risk factor	perioperative β-blockade
ischemic heart disease	yes
congestive heart failure	yes
insulin-dependent diabetes	yes
high risk surgery	probably yes
renal insufficiency	probably yes
impaired general condition	yes, if caused by cardiac disease

such as atenolol 50 mg orally once a day (10), bisoprolol 5 mg once a day (43) or metoprolol 25 mg twice a day (54). It is advised to start this therapy 30 days preoperatively and to aim at a heart rate ≤ 65 beats/min with a systolic blood pressure > 100 mm Hg. In patients who are already on β-blocking therapy, it is suggested to adjust the dosage in order to reduce the heart rate to ≤ 65 beats/min. Effects of β-blockade should be evaluated after 1 week, and if necessary the dosage should be

Table 4

Risk factors according to the Revised Risk Index (ref. 55)

1. high risk surgery	thoracic surgery vascular surgery intraabdominal surgery
2. coronary disease	myocardial infarction angina pathologic Q-wave on ECG positive stress test residual angina after coronary surgery or PTCA nitrate medication
3. cerebrovascular disease	TIA or CVA
4. insulin-dependent diabetes mellitus	
5. chronic renal insufficiency	creatinin > 177 μmol/l

PTCA = percutaneous transluminal angioplasty ; TIA = transient ischemic attack ; CVA = cerebrovascular accident.

adapted. Optimal β-blocking is achieved when heart rate at rest is ≤ 65 beats/min and when maximal heart rate at exercise is < 110 beats/min.

Table 5

Contraindications for perioperative β -blockade

absolute contraindications
1. hemodynamic instability
2. heart rate < 55 beats / min
3. 2nd or 3th degree AV block without pacemaker
4. sick sinussyndrome without pacemaker
5. systolic blood pressure < 100 mm Hg
6. acute cardiac failure
7. left ventricular ejection fraction < 30%
8. acute bronchospasm
9. MAO - inhibitors in within 2 weeks before surgery
10. cocaine-induced myocardial ischemia
11. allergic reaction to β -blocking drugs
relative contraindications
1. hypotension and rhythm disturbances when patients are treated with :
<i>sotalol, calcium antagonists</i>
<i>digoxine, kinidine, amiodarone, procainamide, disopyramide</i>
<i>propafenon</i>
<i>guanitidines</i>
<i>methylodopa</i>
<i>clonidine, lidocaine, cimetidine</i>
<i>phenothiazines</i>
<i>lithium</i>
2. serious peripheral arterial disease
3. chronic obstructive lung disease and asthma

MAO = monoamino oxidase.

It is not always possible to start the β -blocking therapy 30 days in advance. More frequently, the indication for β -blocking therapy is defined shortly before the surgical procedure is scheduled. In that case, it is advised to administer β -blockade intravenously 30 min before the induction of anesthesia. Here again different regimens are possible : atenolol 5 – 10 mg, metoprolol 2 – 15 mg, or esmolol 1 mg/kg in order to reach a heart rate \leq 65 beats/min and a systolic blood pressure > 100 mm Hg. Perioperatively, β -blockade can be maintained intravenously with atenolol 5 – 10 mg, metoprolol 2 – 15 mg, or esmolol 50-200 mg/kg/min. As soon as oral administration is possible, atenolol 50-100 mg once a day, bisoprolol 5-10 mg, once a day or metoprolol 25-50 mg twice a day can be started. It seems wise to continue the intravenous β -blocking therapy until the oral administration starts to work, this in order to keep heart rate between the given limits. β -blockade should be continued throughout the hospital stay and it is even advised to continue it after discharge (56).

Practical implications for perioperative β -blockade : contraindications for β -blockade

Contraindications for perioperative β -blocking therapy are summarized in Table 5. Acute car-

diac failure and hemodynamic instability remain the major contraindications. β -blocking therapy should be adapted in order to obtain heart rates between 55 and 65 beats / min and a systolic pressure > 100 mm Hg. With the introduction of the cardioselective β -blocking drugs, chronic obstructive lung disease and stable non-active asthma are no longer regarded as a contraindication, but instead are even an indication for the use of β -blocking drugs when present together with coronary artery disease (57, 58). The same is true for patients with chronic congestive heart failure (NYHA class II and III) (59).

It is important to remember that β -blocking drugs, in association with other medications, can precipitate rhythm disturbances and hemodynamic instability (60, 61). The use of cardioselective β -blocking drugs does not increase the frequency of hypoglycemic attacks in diabetic patients (62). Furthermore, β -receptor antagonists have been reported to decrease one-year mortality in elderly diabetics (63). β -blocking therapy does also not interfere with the occurrence and the duration of postoperative ileus (64).

Another point of concern is the possibility of interaction when β -blocking drugs are used in the presence of locoregional anesthesia. Although β -blocking drugs may prolong the effects of local anesthetic drugs (65), most reports mention a beneficial effect on perioperative hemodynamics (66, 67) and advise to continue chronic β -blockade (68).

RESULTS OF THE INTERACTIVE VOTING SESSION

Although the significance of the use of β -blocking drugs in the perioperative period is gaining wide acceptance in anesthesiological literature, little is known on the daily practice of anesthesiologists with regard to the prophylactic use of β -blockers. The interactive voting session aimed to get some more information on this subject. Of the participants at the meeting, 79% were anesthesiologists and 15% were trainees. 62% of the participants worked in a public university hospital, 10% in a public non-university hospital and 23% in a private hospital.

91% of the participants were convinced that β -blockers should be started preoperatively in patients with *known* ischemic heart disease. On the other hand, in patients with *suspected* ischemic heart disease (2 known risk factors) only 83% felt that preoperative β -blocking therapy would be useful. The indication for the prescription of

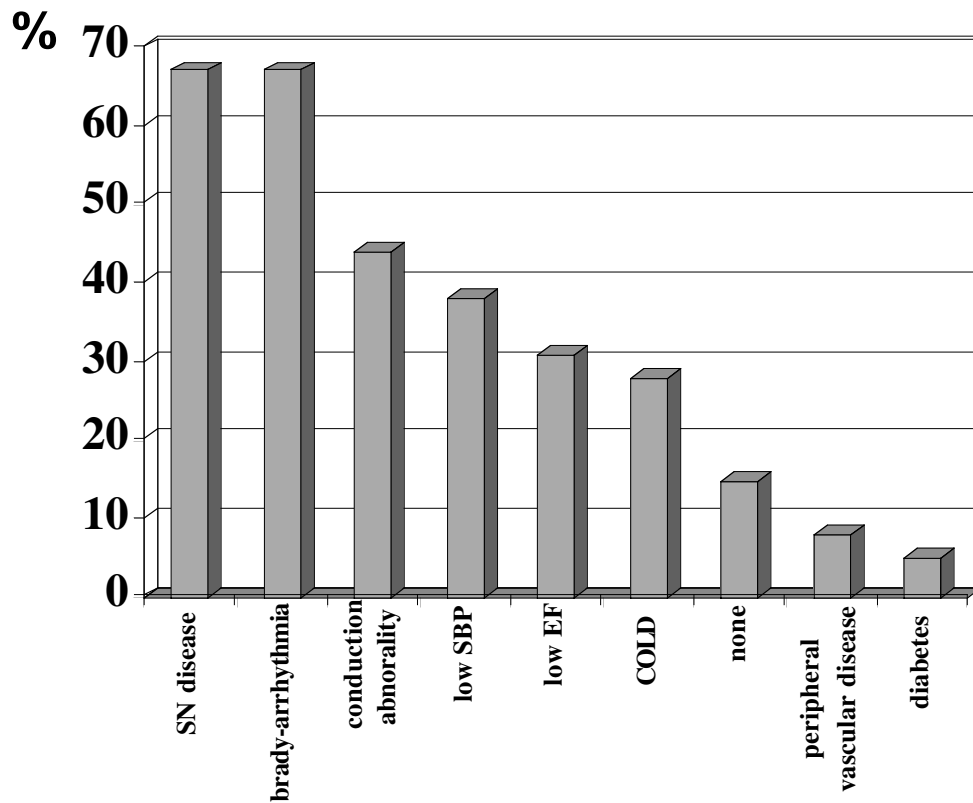


Fig. 4. — Percentage of the different reported contraindications for the preoperative use of β -blockers

β -blockers preoperatively varied. 90% of the participants prescribed β -blockers when the patient was on chronic β -blocking therapy. 38% of the participants considered the prescription of the β -blockers in the perioperative period to be the responsibility of the cardiologists and did so when prescribed by the cardiologists. 38% also considered uncontrolled preoperative hypertension and/or tachycardia to be an indication to start β -blocking therapy preoperatively. The presence of proven or suspected ischemic heart disease, based on the presence of risk factors was considered to be an indication for β -blockers by only 33% of the participants.

One of the major issues with respect to the administration of β -blockers, especially in the perioperative phase, is related to the possible contraindications. Figure 4 shows the different possible contraindications in decreasing order of importance. It appears that rhythm disturbances and conduction abnormalities are considered to be the most important contraindication to the start of β -blockers. An ejection fraction of less than 35%, the presence of a low systolic blood pressure and the existence of chronic obstructive lung disease are considered to be contraindications by about one third of the participants. Severe diabetes and peripheral vascular insufficiency remain a formal contraindication

for only a minority of the anesthetists. 15% believed that there are no contraindications for the use of β -blockers. Most of the anesthesists (93%) select the same drug as the one used in the chronic treatment to use in the perioperative phase. If a new drug has to be started, more than 40% prefer a short-acting β_1 -selective blocker. Intrinsic sympathomimetic activity and route of elimination did not appear to be crucial in the choice of the drug (10%). The choice between the different available β -blockers is summarized in figure 5. Metoprolol and atenolol are most frequently used, which is consistent with the report that intrinsic sympathomimetic activity is not really considered an essential property for this indication.

β -blockers may interact with other drugs used for the treatment of hypertension. 62% of the participants considered that calcium channel blockers constituted a contraindication for the start of β -blocking therapy preoperatively, whereas only 28% had this feeling for the angiotensin converting enzyme inhibitors. Possible interaction between perioperative β -blockade and anesthesia is another point of concern in the literature. However it seems that about 75% of the participants do not adapt the anesthesia technique in patients receiving preoperative β -blockade. Less than 20% avoid hypnotics

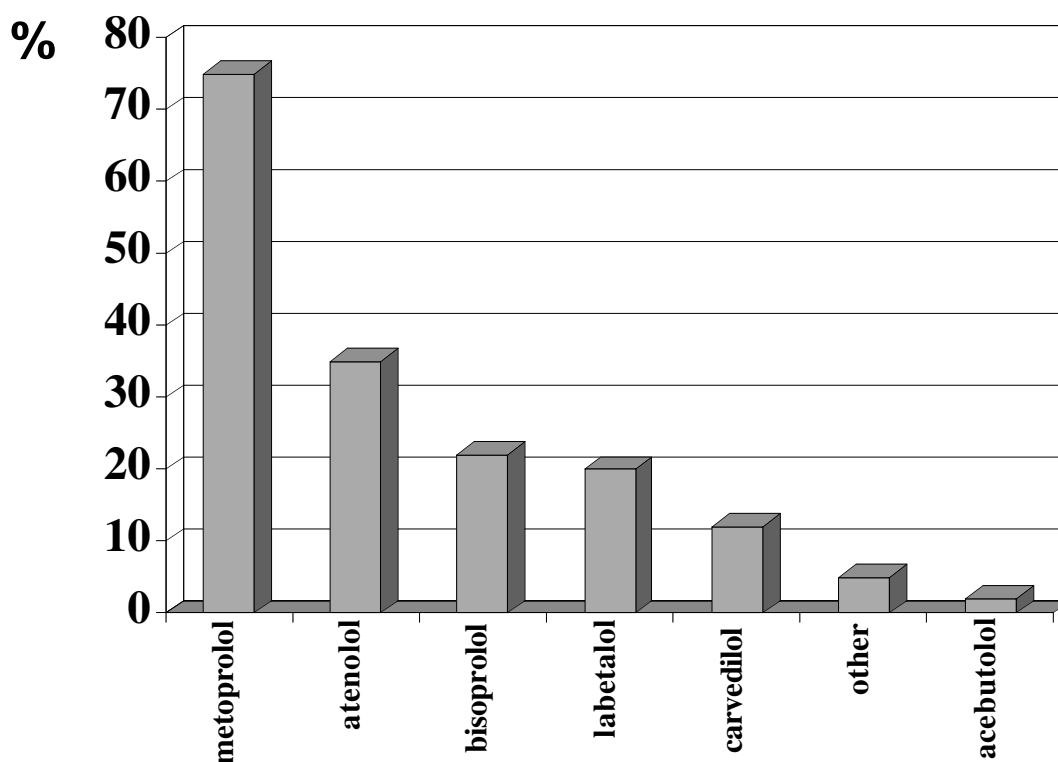


Fig. 5. — Percentage of the different β -blockers used in the perioperative period

or neuromuscular transmission blockers that may cause bradycardia. Only 2% prefer to avoid neuroaxial anesthesia in the presence of β -blocking therapy.

A second part in the discussion on the perioperative use of β -blockers is the administration in the postoperative phase. The first question is when to restart the β -blocking therapy? 80% feel that β -blockers should be restarted as soon as possible. Only 8% of the participants were prepared to wait until gastrointestinal motility was restored. The preferred route of administration in the absence of gastrointestinal motility was intravenously (58%). Only 22% preferred administration through the nasogastric tube. The contraindications for postoperative administration of β -blockers as judged by the participants are shown in Figure 6. As for the preoperative administration, rhythm and conduction abnormalities were considered to represent the most important contraindication. Decreased myocardial function and chronic obstructive airway disease were regarded as a more important contraindication for the postoperative administration of β -blockers as for the preoperative administration. It seems therefore that many anesthesiologists still feel uncomfortable to administer β -blocking drugs in the presence of cardiac disease. Time has come to realize that there are no longer arguments to deprive a patient from the benefi-

cial effects of perioperative β -blocking therapy because cardiac disease is present.

CONCLUSION

The increasing evidence that β -blocking agents may have a favourable effect on perioperative cardiac morbidity and mortality, has led to a changed attitude in the perioperative management of patients with cardiac disease in anaesthesia practice. Recent review articles have focused on the physiology and pharmacology of β -blocking drugs and their interactions with anesthetic agents and techniques (69, 70). Although the notion of the protective effects of β -blocking agents is now well established, there are a number of issues that remain unresolved (39). The optimum timing and duration of β -blocking therapy still is not defined. The different studies have used different protocols and it is not clear which protocol is optimal, or even more, if each protocol is suitable for the different subsets of patients and the different types of surgery. Another question relates to the possible contraindications of β -blocking therapy, especially their use in patients with severely compromised myocardial function. Clearly, further studies will have to refine the strategies on β -blocking therapy in the perioperative setting. For the present we

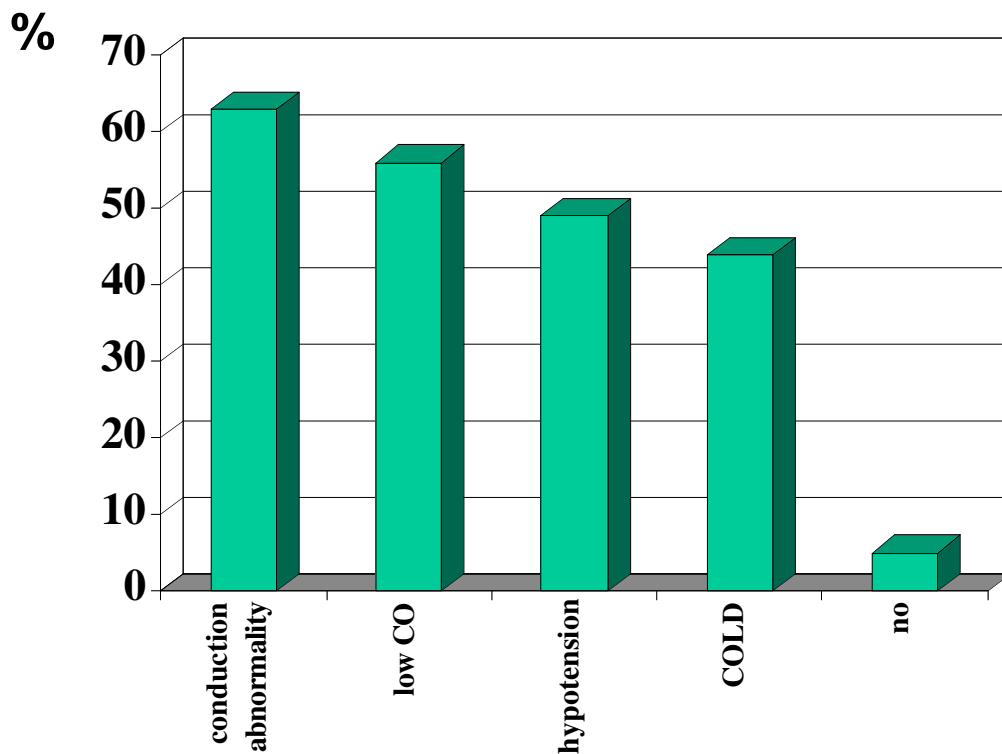


Fig. 6. — Percentage of the different reported contraindications for the postoperative use of β -blockers

know that β -blocking agents are beneficial in the perioperative period; however, the underlying mode of action and the optimal dosage scheme remain to be established.

Appendix

The *Flemish Workgroup of Cardiothoracic and Vascular Anesthesia*: P. Wouters (KUL), S. De Hert (UIA), J. Poelaert (RUG), C. Verborgh (VUB), D. Vlasselaers (KUL), L. Foubert (OLVZ Aalst), M. Suy (AZM), JP. Mulier (AZ St Jan Brugge), J.P. Ory (Virga Jesse, Hasselt), R. De Jongh (ZOL, Genk), D. De Kegel (Heilig Hart Ziekenhuis, Roeselare), C. Devuyt (ASZ, Aalst), R. Barbé (Imeldaziekenhuis, Bonheiden), J.L. Demeere (St-Jan Ziekenhuizen, Brussel), M. Moens (St Elizabethziekenhuis, Ukkel), E. De Lombaerde (Maria Middelaers, Gent)

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