General Anesthesia

Perioperative use of beta-blockers remains low: experience of a single Canadian tertiary institution

[L'usage périopératoire des bêta-bloquants n'est pas fréquent : l'expérience d'un seul centre tertiaire canadien]

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Background: Perioperative beta-blockade appears to reduce morbidity and mortality in non-cardiac surgery, and is recommended by published guidelines. This study explores the frequency of perioperative beta-blockade and identifies factors limiting its use.

Methods: We conducted a prospective analysis of consecutive patients seen by anesthesiologists before major non-cardiac surgery in a single month. Because not all patients undergoing major surgery were seen preoperatively by anesthesiologists, we also performed a retrospective analysis of patients who recently underwent such surgery. Data were collected on demographic information, cardiovascular risk factors, beta-blocker use, and perceived contraindications/barriers to beta-blocker use, using a validated instrument.

Results: The prospective phase studied 222 patients preoperatively, of whom 96 were suitable candidates for perioperative beta-blockade by the American College of Physician guidelines. The retrospective phase studied 200 patients, of whom 63 were suitable candidates, and assessed pre- and postoperative use of beta-blockade. 40.6% and 38.1% of suitable patients received preoperative beta-blockade in the two phases, respectively. Findings were similar in those undergoing vascular surgery, suggesting that perception of perioperative risk did not influence the decision to use beta-blockade. Beta-blockers were not prescribed preoperatively because of lack of knowledge about contraindications to beta-blockade, and anesthesiologist reluctance to prescribe oral medication to outpatients.

Discussion: Use of preoperative beta-blockade among suitable candidates appears to be approximately 40%. Anesthesiologists started preoperative beta-blockers infrequently even in patients without contraindications. These findings suggest that educating anesthesiologists about the perioperative use of beta-blockade may increase the use of this potentially beneficial strategy.

Objectif : Le bêta-blocage périopératoire semble réduire la morbidité et la mortalité en chirurgie non cardiaque et est recommandé par des normes publiées. La présente étude explore la fréquence de bêta-blocage périopératoire et identifie les facteurs qui en limite l'usage.

Méthode : Nous avons réalisé une analyse prospective de patients vus consécutivement par des anesthésiologistes avant une opération non cardiaque majeure au cours d'un seul mois. Comme tous les patients n'étaient pas vus par l'anesthésiologiste avant une opération majeure, nous avons aussi fait une analyse rétrospective des patients qui ont récemment subi une telle opération. Nous avons recueilli, à l'aide d'un instrument validé, des données sur les caractéristiques démographiques, les facteurs de risque cardiovasculaire, l'usage de bêta-bloquants et les contre-indications/barrières perçues à l'usage de bêta-bloquants.

Résultats : La phase prospective a porté sur l'évaluation préopératoire de 222 patients, dont 96 étaient des candidats admissibles à un bêta-blocage périopératoire selon les American College of Physician guidelines. La phase rétrospective a porté sur 200 patients, dont 63 candidats au bêta-blocage, et évalué l'usage préopératoire et postopératoire du bêta-blocage. Parmi les patients admissibles, 40,6 % et 38,1 % ont respectivement reçu un bêta-blocage préopératoire au cours des deux phases. Les résultats ont été similaires à ceux des patients de cardiologie, ce qui laisse croire que la perception du risque périopératoire n'influence pas la décision d'utiliser le bêta-blocage. Les bêta-bloquants préopératoires n'ont pas été prescrits à cause d'un manque de connaissances sur les contre-indications et à cause d'une réticence de l'anesthésiologiste à prescrire une médication orale aux patients ambulatoires.

Discussion : L'usage préopératoire de bêta-blocage chez des candidats admissibles est d'environ 40 %. Les anesthésiologistes ne l'u-

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tilisent pas souvent avant l'opération même dans les cas sans contre-indications. On peut donc dire que si les anesthésiologistes connaissaient mieux son usage périopératoire, ils pourraient utiliser davantage cette stratégie potentiellement bénéfique.

PERIOPERATIVE cardiovascular events occur in up to 8% of patients undergoing major non-cardiac surgery, especially those with known coronary heart disease or multiple cardiac risk factors.¹⁻⁴ In North America, more than three million such patients undergo non-cardiac surgery annually, and the costs attributed to perioperative cardiovascular events exceed \$30 billion CDN per year.⁵ Since responsibility for patients undergoing major surgery is shared by surgeons, internists, anesthesiologists and family physicians, all of these groups have traditionally been interested in improving the quality of perioperative care.

Perioperative beta-adrenergic receptor blockade has been shown to improve several important patient outcomes including myocardial infarction and mortality.⁶⁻¹¹ Accordingly, clinical practice guidelines recommend the use of perioperative beta-blockade in high-risk patients undergoing major non-cardiac surgery, especially vascular surgery.^{12,13}

There are few published data describing the frequency with which beta-blockers are administered to patients undergoing major non-cardiac surgery. However, clinical experience suggests these agents may be underutilized, and barriers to increasing perioperative use of beta-blockade have not been described. We designed this study to determine the frequency of perioperative beta-blockade in patients undergoing major non-cardiac surgery, and to identify factors that might be limiting its use.

Methods

Prospective phase

The Institutional Review Board at the University of Alberta approved this study. First, a prospective survey of anesthesiologists who were evaluating patients in the preanesthetic care unit was conducted at a single Canadian tertiary care institution. Anesthesiologists were asked to complete one questionnaire for each eligible patient. The questionnaire included items for demographic information (but no identifying characteristics such as name, address or date of birth), cardiovascular risk factors, beta-blocker use, and perceived contraindications to beta-blocker use. Anesthesiologists were asked if they had recommended perioperative beta-blockade for each patient and the reason(s) why or why not.

Eligible patients for the prospective phase included consecutive patients seen in the preanesthetic care unit during the four-week study period. Patients undergoing major non-cardiac surgery (*ip*, non-cystoscopic urological, intrathoracic, major vascular, or major orthopedic surgery) were eligible for inclusion.

The study questionnaire was validated using standard techniques.¹⁴ Questionnaire items were developed by an anesthesiologist (S.R.) and an internist (M.T.), and reviewed with colleagues to establish face and construct validity. The instrument was evaluated for accuracy (criterion validity) and test-retest reliability in a group of three simulated patients by six anesthesiologists who did not participate in the study. Each anesthesiologist completed the instrument twice for each simulated patient (eight weeks apart). Accuracy on the study items was 99.3% overall, and was 100% for beta-blocker use/non-use. Test-retest reliability was assessed using the kappa statistic, which was 0.87 for the three binary variables considered (beta-blocker use/non-use, decision to start beta-blockers preoperatively, presence/absence of coronary disease), indicating excellent reproducibility.

Retrospective phase

It was anticipated that not all candidates for perioperative beta-blockade would be seen in the preanesthetic care unit, and also that changes to perioperative medications might be made after the pre-admission visit (in hospital or at an appointment with another consultant). Therefore, an additional sample of 200 patients who had recently undergone major surgery was evaluated retrospectively, with emphasis on the high-risk population undergoing vascular procedures. Data from the computerized anesthesia recording system at the study institution were used to identify the names of consecutive patients who had recently undergone major surgery in the following distribution: 125 who underwent major vascular procedures; and 75 individuals who had undergone a major urologic, *ip* or thoracic procedure (25 of each). Because of the deliberate over-representation of patients undergoing vascular surgery in the retrospective phase, no statistical comparison has been made with the prospectively collected data.

Patient charts were reviewed and data were extracted by a single investigator (I.R.) using a standardized form. Information on patient demographics, cardiovascular risk factors, beta-blocker use (preoperative, intraoperative, postoperative), and contraindications to beta-blocker use (history of reversible airways disease, wheeze on physical examination, second or third degree heart block, decompensated congestive heart

failure, heart rate < 60 beats·min⁻¹) was collected. To maintain patient confidentiality, no information which could be used to identify individual subjects was included in the working copy of the study database.

In both phases of the study, American College of Physician (ACP) guidelines¹³ were used to determine which patients were candidates for perioperative beta-blockade. These guidelines specify that patients with known coronary disease (previous myocardial infarction, angina, or previous positive stress test) and those with two or more of the following risk factors (age ≥ 65 yr, known hypertension, current smoking, history of hypercholesterolemia, or diabetes mellitus) should be considered for perioperative beta-blockade. In the current study, we also considered those with previous coronary revascularization to have coronary disease.

Statistical analysis

Variables were described using mean ± SD or proportions. Proportions were compared using Chi-square tests where appropriate. Analyses were performed using SAS 8.2 software (SAS Corporation, Cary, NC, USA).

Results

Information was collected on 222 consecutive patients in the prospective phase and 200 in the retrospective phase of the study. Study forms were completed for all 222 patients in the prospective phase. Demographic and clinical characteristics of these individuals are shown in Table I.

Prospective phase

According to the ACP criteria,¹³ perioperative beta-blockade should have been considered in 121/222 (54.5%) of patients. Of these, 25 (20.7%) had contraindications, including previous intolerance to beta-blockade (0.8%), third degree heart block (0.8%) history of reversible airways disease (5.0%), wheezing on physical examination (1.6%), and heart rate < 60 beats·min⁻¹ (14.0%; categories not mutually exclusive). Thus, 96 candidates suitable for perioperative beta-blockade remained.

In 34/96 (35.4%) of suitable candidates, beta-blockers were being taken at the time of the clinic visit, and beta-blockers were started preoperatively in an additional five such individuals, leaving 57 (59.4%) suitable candidates who apparently did not receive preoperative beta-blockade (Table II). Among these 57 patients, 12 had a blood pressure greater than 160/100, and 34 had a blood pressure greater than 140/80, suggesting that beta-blockade might have improved control of hypertension in addition to

TABLE I Clinical characteristics of study participants

	Prospective n = 222	Retrospective n = 200
Age	55.6 ± 22.7	67.5 ± 11.5
Type of surgery		
General (<i>ip</i>)	45 (20.3%)	25 (12.5%)
Head and neck	21 (9.5%)	0
Major vascular	37 (16.7%)	125 (62.5%)
Orthopedic	48 (21.6%)	0
Thoracic	12 (5.4%)	25 (12.5%)
Urologic	35 (15.8%)	25 (12.5%)
Other	24 (10.8%)	0
Seen in preanesthetic care clinic	222 (100%)	139 (69.5%)
Known coronary disease	42 (18.9%)	90 (45%)
Angina	20 (9.0%)	52 (26%)
Previous myocardial infarction	18 (8.1%)	32 (16%)
Positive exercise stress test	3 (1.4%)	5 (2.5%)
Q waves on electrocardiogram	9 (9.0%)	20 (10%)
Previous coronary revascularization	13 (5.9%)	25 (12.5%)
Other	10 (4.5%)	0
History of hypertension	115 (51.8%)	119 (59.5%)
History of hyperlipidemia	37 (16.7%)	58 (29.6%)
Diabetes mellitus	34 (15.3%)	24 (12%)
Current smoker	66 (29.7%)	105 (52.5%)
Perioperative beta-blockade recommended by ACP	121 (54.5%)	142 (71%)
Previously failed a trial of beta-blockade	1 (0.5%)	1 (0.5%)
Systolic blood pressure (mmHg)	135 ± 20	131 ± 19
Diastolic blood pressure (mmHg)	78 ± 12	78 ± 13
Heart rate (per minute)	75 ± 13	72 ± 14
On beta-blocker*	54 (24.3%)	55 (27.5%)
Started on beta-blocker at clinic visit	6 (2.7%)	0
Started on beta-blocker postoperatively	n/a	46 (23%)

*At time of clinic visit (prospective data) or at time of admission to hospital (retrospective data). n/a = not applicable; number (percentage); mean ± SD. ACP = American College of Physicians.

reducing perioperative risk. A list of the explanations provided by anesthesiologists for the non-prescription of beta-blockade to suitable candidates appears in Table III. The most common reason given for non-prescription was the absence of documented coronary disease. Other reasons cited included the concomitant use of other medications such as angiotensin-converting enzyme inhibitors or calcium channel blockers, reluctance to prescribe medications to outpatients, and concern that beta-blockade might precipitate hypoglycemia in diabetic patients.

To determine whether the likelihood of instituting beta-blockade was influenced by perceived cardiovascular risk, we considered subgroups defined by pre-existing coronary disease and the need for vascular

TABLE II Rates of beta-blockade use and contraindications

<i>Prospective phase</i>		
Overall (<i>n</i> = 222)	On beta-blocker*	54/222 (24.3%)
	Contraindication(s)†	30/162 (9.0%)
	Started on beta-blocker at clinic visit	6/222 (2.7%)
Ideal candidates‡ (<i>n</i> = 96)	Taking beta-blocker at clinic visit	34/96 (35.4%)
	Started on beta-blocker at clinic visit	5/96 (5.2%)
	Overall perioperative beta-blocker use	39/96 (40.6%)
Vascular surgery (<i>n</i> = 37)	On beta-blocker *	17/37 (45.9%)
	Started on beta-blocker at clinic visit	1/37 (2.7%)
	Overall perioperative beta-blocker use	18/37 (48.6%)
<i>Retrospective phase</i>		
Overall (<i>n</i> = 200)	On beta-blocker *	55/200 (27.5%)
	Contraindication(s)†	49/99 (49.5%)
	Started on beta-blocker postoperatively	46/200 (23%)
Ideal candidates‡ (<i>n</i> = 63)	Taking beta-blocker preoperatively	24/63 (38.1%)
	Started on beta-blocker postoperatively	16/63 (25.4%)
	Overall perioperative beta-blocker use	40/63 (63.5%)
Vascular surgery (<i>n</i> = 125)	On beta-blocker *	38/125 (30.4%)
	Started on beta-blocker postoperatively	42/125 (34%)
	Overall perioperative beta-blocker use	80/125 (64.0%)

*At time of clinic visit (prospective data) or at time of admission to hospital (retrospective data); † Among those not receiving perioperative beta-blockade. Contraindications included: history of reversible airways disease, wheezing on physical examination, second or third degree heart block, decompensated congestive heart failure, heart rate < 60 beats·min⁻¹; ‡ Suitable candidates were those in whom the use of perioperative beta-blockade is recommended by the American College of Physicians (ACP) criteria, and in whom there was no contraindication.

surgery. Findings were similar when only the 37 patients undergoing vascular surgery were considered. Specifically, 17 (45.9%) were already receiving beta-blockers, and an additional 11 (29.7%) had contraindications to these medications or had a heart rate < 60 beats·min⁻¹. One patient had a beta-blocker started during the clinic visit. Thus, among patients undergoing vascular surgery, preoperative beta-blockade was used in 14/26 (53.9%) who were apparently suitable candidates. This was not significantly different from the frequency of perioperative beta-blocker use in suitable candidates undergoing other types of surgery ($P = 0.50$). Although subjects with coronary disease and no contraindications were more likely to receive beta-blockade at the time of the clinic visit than those without coronary disease (72% *vs* 19%, $P < 0.001$), the frequency with which beta-blockers were started by anesthesiologists was low in both groups (13% *vs* 7%, $P = 0.51$).

TABLE III Relative frequency of anesthesiologists' explanations for not prescribing perioperative β -blockade in suitable candidates

- No documented history of coronary disease (18%);
- Concomitant use of calcium channel blocker, angiotensin-converting enzyme inhibitor or alpha-adrenergic blocker (18%);
- Belief that "chronic obstructive pulmonary disease" constitutes contraindication to beta-blockers (11%);
- Concern that patient was receiving too many medications already (9%);
- Concern about precipitating hypoglycemia in diabetic patient (9%);
- Concern about prescribing medications to patient that anesthesiologist would not be seeing again (9%).

There were 57 suitable candidates who did not receive perioperative beta-blockade in the current study. These subjects met the American College of Physicians (ACP) criteria for perioperative use of beta-blockade and did not have a contraindication to its use. An explanation for beta-blocker non-use was not provided in all cases.

Retrospective phase

To ensure that data collected in the preanesthetic care unit reflected medications actually received in the perioperative period, we retrospectively collected information from 200 randomly selected patients who underwent major surgery at our institution. Demographic and clinical characteristics of these individuals appear in Table I.

Among the 200 patients, 63 were suitable candidates for perioperative beta-blockade. In this latter group, 24/63 (38.1%) received beta-blockers preoperatively, and an additional 16/63 patients (25.4%) were started on beta-blockers postoperatively. Thus, 40/63 (63.5%) of suitable candidates received beta-blockade at some time during the perioperative period.

Postoperative beta-blockade was started in 16/39 (41.0%) of patients who appeared to be suitable for this strategy. However, beta-blockers were also started postoperatively in 30 patients in whom their use was not specifically recommended by the ACP guidelines ($n = 6$), who had a contraindication to their use ($n = 28$) or both ($n = 4$).

Most of the patients in whom beta-blockade was started postoperatively (42/46, 91.3%) had undergone vascular surgery. Thus, 34% (42/125) of patients undergoing vascular surgery were started postoperatively on beta-blockers, and a total of 64% (80/125) received beta-blockade at some time during their hospital stay. Postoperative beta-blockade was started relatively infrequently among patients undergoing other types of surgery (4/75, 5.3%).

Discussion

Randomized clinical trials have shown that perioperative beta-blockade significantly reduces cardiac morbidity and mortality.⁶⁻¹⁰ Consequently, several major organizations recommend the use of this strategy in all high-risk patients undergoing major non-cardiac surgery.^{12,13} However, we found that preoperative use of beta-blockers in suitable patients with no contraindications was approximately 40%, a figure that was consistent in the two phases of our study.

Anesthesiologists started preoperative beta-blockade infrequently in the preanesthetic care clinic, even in patients who appeared suitable candidates for this strategy and had known coronary disease. Interestingly, use of preoperative beta-blockade was similar in patients undergoing vascular surgery (who are known to be at high risk of cardiovascular events), compared with those undergoing other types of surgery. This suggests that anesthesiologists' perceptions of perioperative risk may not influence the decision to prescribe beta-blockers.

Data on the perioperative use of beta-blockade are limited. A retrospective American study of 158 patients undergoing non-cardiac surgery found that the prevalence of beta-blocker use among apparently suitable patients was 37%, similar to our results.¹⁵ Likewise, a recent retrospective Canadian study of 143 patients undergoing general surgery found that 39% of those with coronary disease received perioperative beta-blockade.¹⁶ However, these articles did not explore barriers to the use of perioperative beta-blockade, and the former did not differentiate between pre- and postoperative use of beta-blockers. A third study found that the frequency of perioperative beta-blockade in patients seen in consultation by internists before non-cardiac surgery was only 11% but most participants were at low cardiovascular risk.¹⁷ Finally, Schmidt *et al.*¹⁵ concluded that the observed non-use of beta-blockade would be expected to result in at least 60 preventable deaths annually at their institution. In our opinion, this emphasizes the potential value of devising strategies to increase the use of this potentially effective therapy.

Why is the use of preoperative beta-blockade so low? In the current study, reasons given by anesthesiologists for non-prescription varied, but included concerns about the likely risk and/or benefit associated with therapy. Anesthesiologists also cited concern about prescribing oral medications to patients without scheduled follow-up. Although we did not attempt to determine whether anesthesiologists were unaware of the clinical practice guidelines recommending perioperative beta-blockade, this may have been a factor in some cases. Finally, even if aware of the practice guidelines, anesthesiologists' perceptions about the value of treatment may have been influenced by knowledge of an on-going trial (the Perioperative Ischemic Evaluation - POISE - study) which is randomizing patients undergoing non-cardiac surgery to perioperative beta-blockade or placebo.

While prescription of preoperative beta-blockade was infrequent, the retrospective phase of our study suggests that a substantial proportion of patients are started on beta-blockers postoperatively, especially those undergoing vascular surgery. Although postoperative beta-blockade might prevent cardiovascular events compared with not starting beta-blockers at all, it is important to note that this is unproven. Therefore, it seems reasonable that perioperative beta-blockade should include both pre- and postoperative use of beta-blockers.

Previous work suggests that specific interventions may increase the proportion of patients who receive perioperative beta-blockade. For instance, a recent uncontrolled Canadian study found that an interven-

tion aimed at anesthesiologists, internists, family physicians and postanesthesia care unit staff was associated with perioperative beta-blockade rates of 69%.¹⁸

Armanious *et al.*¹⁸ chose to have prescriptions for oral beta-blockers written by internists - which may have been important given the apparent reluctance of anesthesiologists to prescribe them in the current study. Some of the reasons given by anesthesiologists in our study for non-prescription of beta-blockers (concomitant use of other medications, potential for hypoglycemia, history of "chronic obstructive pulmonary disease", etc.) do not constitute true contraindications. These observations suggest that use of perioperative beta-blockade might be increased by a multidisciplinary approach and education directed at anesthesiologists, as well as family physicians, internists and surgeons.

However, interventions that rely simply on passive knowledge transfer may be insufficient, since many anesthesiologists consider themselves to be aware of recent literature on perioperative beta-blockade.¹⁹ In addition to targeted educational programs, Armanious *et al.* provided information sheets to patients and their family physicians, which may have improved long-term compliance with therapy. Based on lessons learned from other strategies aimed at changing physician behaviour, real-time reminders to prescribe beta-blockade and practice audits involving comparison with peers may also be beneficial.²⁰ Finally, pre-printed protocols appear to increase utilization rates of beta-blockers after acute myocardial infarction,²¹ and should therefore be considered for perioperative beta-blockade as well.

The current study has a number of limitations which should be considered. First, it may have been preferable to follow those patients seen in the preoperative clinic into the postoperative period rather than obtaining two separate samples of patients. However, all data were contemporaneous and from a single institution, suggesting that this is unlikely to have affected our results. Second, the retrospective phase of the study was conducted by chart review, the limitations of which are well described. However, we attempted to minimize bias by randomly selecting cases from the operating room log, and with data extracted from the chart in standardized fashion by a single investigator. Although participating in the survey may have influenced the practice of anesthesiologists, this would have been expected to increase the use of beta-blockade, suggesting that our conclusions are unlikely to have been affected by this potential bias. Third, although other therapies such as alpha-2 adrenergic agonists might also improve perioperative outcomes,²²

we did not collect information on their use in the current study. Fourth, we did not measure the number of doses of beta-blocker that patients received, and thus cannot determine the number of patients that received on-going beta-blockade as recommended by Mangano *et al.*⁸ Fifth, this was a single centre study, and collecting data from multiple tertiary centres would have improved the external validity of our findings. Sixth, asking anesthesiologists to specify patient characteristics that would have made them more likely to prescribe beta-blockers would have been potentially informative. Unfortunately we did not collect this information in the current work.

Despite these potential limitations, we developed and validated our instrument in accordance with accepted techniques, studied consecutive patients in the prospective phase, and randomly selected participants for the retrospective phase. In addition, all charts in the retrospective phase were reviewed by a single physician, which in our opinion is likely to have improved the quality of the data. We therefore believe that bias related to study design is unlikely to have significantly influenced our findings.

In summary, perioperative beta-blockade was used in approximately 40% of suitable patients undergoing non-cardiac surgery in a Canadian tertiary centre. Our data suggest that use of perioperative beta-blockade might be increased by educating physicians about the potential benefits of this strategy, as well as contraindications to its use.

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