US and European Societies Issue New CV Guidelines for Noncardiac Surgery

Michael O'Riordan | August 01, 2014

WASHINGTON, DC and SOPHIA ANTIPOLIS, FRANCE — The major cardiology societies in the US and Europe have published new recommendations for the cardiovascular management of patients undergoing noncardiac surgery[1,2], including clarifying the role of beta-blocker therapy in the post-**DECREASE** era.

In the 2014 joint guidelines from the **European Society of Cardiology** and **European Society of Anesthesiology** (ESC/ESA), the new recommendations state that beta-blockers are not recommended in patients without clinical risk factors, given that the drugs do not decrease the risk of cardiac complications and "may even increase this risk." A retrospective cohort study also suggested beta-blockers in these low-risk patients might increase the risk of death.

"One cannot justify exposing low-risk patients to potential adverse effects in the absence of proven benefit," write ESC/ESA guideline committee chair **Dr Steen Dalby Kristensen** (Aarhus University Hospital, Skølby, Denmark) and colleagues August 1, 2014 in the *European Heart Journal*. "The issue remains debatable in intermediate-risk patients, ie, those with one or two clinical risk factors. Increased mortality following preoperative beta-blocker withdrawal has been reported in four observational studies."

In the US, the **American Heart Association** and **American College of Cardiology** (AHA/ACC) also tackle the beta-blocker question. Like the Europeans, the AHA/ACC recommends beta-blockers be continued in patients undergoing surgery if they have been taking the drugs chronically (class I, level of evidence B). For those with intermediate- or high-risk myocardial ischemia documented prior to surgery, the AHA/ACC states it is reasonable to begin perioperative blockade (class IIb, level of evidence C). For those with three or more risk factors, such as diabetes, heart failure, or coronary artery disease, it is also reasonable to begin beta-blockers prior to surgery (class IIb, level of evidence B).

The US guidelines, also published today in the *Journal of the American College of Cardiology* and *Circulation*, state that in patients with no risk factors, starting beta-blockers in the perioperative setting provides unknown benefit, especially if a long-term indication for beta-blockade is not noted.

Speaking with **heart*wire*** , chair of the AHA/ACC writing committee **Dr Lee Fleisher** (University of Pennsylvania Health System, Philadelphia) said the guidelines reaffirm that stopping beta-blocker therapy in the perioperative period is harmful. "We also downgraded some of the beta-blocker recommendations," said Fleisher. "We felt that you could give beta-blockers to high-risk patients but we downgraded that recommendation from IIa to IIb."

So, Why the Change?

Previously, the 2009 ESC guidelines, which were chaired by **Dr Don Poldermans**, formerly of Erasmus Medical Center, Rotterdam, the Netherlands, awarded beta-blockers a class I indication in patients with established coronary artery disease or ischemia on a preoperative stress test or in patients undergoing high-risk surgery. They were a class IIa indication in patients undergoing intermediate-risk surgery. In the US, the recommendations, as noted by Fleisher, were rated IIa.

The clinical guidelines, both in the US and Europe, based previous recommendations partly on data from the **Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echo** (DECREASE) studies. Poldermans, for his part, published the first **DECREASE** paper in 1999 on the use of **bisoprolol** and also authored subsequent DECREASE studies, including **DECREASE IV,** which addressed the perioperative use of beta-blockers.

As has been reported extensively by **heart*wire*** and other media outlets, Poldermans was fired for violations of academic integrity, including the falsification of results, and resigned from the ESC Committee for Practice Guidelines. Subsequent investigations into his research have questioned the validity of his findings, particularly the DECREASE studies. To **heart*wire*** , Fleisher said a separate evidence review committee (ERC) was responsible for reviewing the literature to address key clinical questions, including those related to the use of perioperative beta-blockers in

noncardiac surgery. This was important given the Poldermans controversy.

"The evidence-review committee reviewed all of the literature, and we really did a lot of sensitivity analyses to look at the findings with and without the Poldermans data," Fleisher told **heart*wire*** . "The data are controversial but still exist in the literature. They've never been retracted. We felt it was important to answer the question with and without those data. The evidence review committee was an independent body, and they really did an excellent job looking at all of these questions."

For the use of beta-blockers in high-risk patients, Fleisher said the strength of evidence is weakened without the Poldermans data—hence, the downgrade—but there still exist nonrandomized data to support its IIb recommendation.

In the new European guidelines, the writing committee excluded the DECREASE studies from the paper and did not use them to inform its new recommendations. In the US, the AHA/ACC writing committee included the DECREASE studies in its sensitivity analyses but also excluded the studies from its report and did not include the findings in the new clinical practice guidelines.

In Europe, beta-blockers have also been downgraded. They should be continued in patients currently receiving the medication (class I, level of evidence B) and can be considered preoperatively in patients with two or more cardiovascular risk factors scheduled for high-risk surgery (class IIb, level of evidence B). In addition, beta-blockade can be considered in patients with known ischemic heart disease or myocardial ischemia (class IIb, level of evidence B).

What About the Role of Statins?

Regarding statins, Fleisher said the ACC/AHA recommendations have not changed much because the DECREASE studies, which tested statins in the perioperative setting, were never used as the sole basis for past clinical guidelines. Most of the data supporting the use of statins in this setting are taken from observational studies, noted Fleisher, but two studies from Poldermans et al, which tested the impact of **fluvastatin** in the perioperative period, showed significant improvement in major adverse cardiac events (MACE) among high-risk patients and a trend toward benefit in intermediate-risk benefit.

"When you take the Poldermans's studies away, there is still a body of evidence that says you shouldn't withdraw statins and it might be reasonable to use statins in patients undergoing surgery."

Specifically, statins should be continued in patients taking the drugs who are scheduled for noncardiac surgery (class I, level of evidence B). Perioperative statin use is deemed reasonable in patients undergoing vascular surgery (class IIa, level of evidence B) and may be considered in patients with indications for statin therapy who are undergoing elevated-risk procedures (class IIb, level of evidence C).

In Europe, the ESC/ESA also recommends the perioperative continuation of statins in patients already receiving the lipid-lowering agents (class I, level of evidence C) and says that they can be considered in patients undergoing vascular surgery, ideally at least two weeks before the procedure (class IIa, level of evidence B).

Commenting on these recommendations for **heart*wire*** , **Dr Darrel Francis** (Imperial College London, UK) believes the US guidelines got it wrong with regard to statins. He noted they based the recommendations on a 100-patient trial that randomized vascular-surgery patients to either **atorvastatin** or placebo for six months, a trial that reported a significant reduction in the risk of MACE. A Cochrane analysis later pooled data from three studies, including this atorvastatin trial, performed by **Dr Anai Durazzo** (University of São Paulo, Brazil).

"For over six months, the outcomes data of one trial, Durazzo et al, have been publicly known to be impossible," Francis told **heart*wire*** . "It claimed to have full follow-up of 50 patients per arm, and no exclusions, meaning each patient is exactly 2% of their trial arm. Unless patients are split into pieces, the stated 91.4% and 73.5% event-free survival rates are impossible. Worse, the survival graph and numerical data presented do not match."

What Else Is New?

In terms of the overall recommendations for managing patients undergoing noncardiac surgery, Fleisher said the new guidelines collapse the distinction between intermediate- and high-risk patients, making the same recommendations for patients who fall within either category. In addition, the guidelines utilize the **Revised Cardiac Risk Index** (RCRI) as the primary tool for assessing cardiac risk, as well as the **American College of Surgeons National Surgical Risk Calculator** (NSQIP) to estimate the likelihood of unfavorable outcomes after surgery.

"We also discuss in this document about how the decision sometimes is not to have surgery," said Fleisher, "and maybe have the alternative, which is palliative care. We also want to really emphasize the importance of shared decision making, which is a big issue these days."

There is also some guidance on the timing of elective noncardiac surgery. Elective noncardiac surgery should be delayed 14 days after balloon angioplasty (class I, level of evidence C) and bare-metal-stent implantation (class I, level of evidence B). Surgery should be delayed one year following the implantation of a drug-eluting stent (class I, level of evidence B) but may be considered after 180 days if the risk of further delay is greater than the risk of ischemia and stent thrombosis.

"We used to say you had to wait a year, but we now think 180 days is reasonable," said Fleisher.

The Process Going Forward

Dr Magnus Ohman (Duke University Medical Center, Durham, NC), a member of the ACC/AHA writing committee, said the update takes a new look at the data since the last set of recommendations, although not a lot has changed from previous guidelines. It provides direction on antiplatelet therapy in patients undergoing urgent and nonemergent noncardiac surgery, including when to continue and when to stop antiplatelet therapy. Like Fleisher, he said the new recommendations are clearer in defining the risks of surgery and the risk factors of the patient.

"The other aspect of this is the debacle related to the academic fraud," said Ohman. "Here, we took a new approach, and we'll see more of this as time goes on, with the committee performing a systematic review of all the beta-blocker data. This will be published as a separate paper."

For Francis, who has repeatedly challenged the European societies on their recommendations for beta-blockers and performed a meta-analysis showing that perioperative beta-blockers given to patients undergoing noncardiac surgery increased the risk of death by 27%, the whole process is flawed. He noted that previous editorials have defended the DECREASE family of studies and that some of the meta-analyses forming the basis of clinical recommendations are based on flawed trials.

"We must learn from this," said Francis. "The guideline writers, being those who scrutinize the science most carefully, will generally be the first to spot problems. Instead of being forced to acquiesce in silence, they should be given the right—or even the responsibility—to speak out publicly and immediately. Our entire community must rise to the task, recognizing our shared responsibility to deal with unreliable science before it can interfere with patient care."

Kristensen reports speaker, honoraria, consultant, advisory-board, and/or committee-member fees from AstraZeneca, Boehringer Ingelheim, Eli Lilly, Pfizer, Bayer Healthcare, the Medicines Company, Bristol-Myers Squibb, Menarini, and Biotronic and research funding to his institution from AstraZeneca. Fleisher reports no conflicts of interest. Disclosures for the coauthors are listed in the papers. Francis reports no conflicts of interest. Ohman reports consulting for Abiomed, AstraZeneca, Daiichi-Sankyo, Gilead Science, Jannsen Pharmaceuticals, Pozen, and Sanofi.

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