VEITH SYMPOSIUM 2015

When Are Beta Blockers Helpful With Vascular Patients and Vascular Procedures: In What Dose And With What Precautions?

Mark L. Friedell, MD
University of Missouri-Kansas City

November 20, 2015

Background

- The use of perioperative beta blockade in non-cardiac surgery has been controversial for decades
- The literature includes outcomes from vascular and general surgery and other surgical disciplines in retrospective observational series, randomized controlled trials, and meta-analyses.

Disclosures

None

Nonemergent

Unstable angina
Heart disease > vascular disease
Severe CHF
Stable angina
Compensated CHF
Eagle risk factors
No significant disease
Normal provocative test

Emergent

VASCULAR SURGERY

INDICATED

OPERATE
1) Assume some CAD
2) B-Blockers
3) Optimize anesthesia

Major CAD Predictors

OPERATE
1) Assume some CAD
2) B-Blockers
3) Optimize anesthesia

HISTORY / PE +/- Provocative test (Usually unnecessary)

Retrospective multicenter analysis of 782,969 NCS patients from 329 hospitals
In-hospital death viewed with a risk assessment tool
For patients with >2 risk factors, BB clearly beneficial
For patients with <2 risk factors, BB provided no benefit and possible harm

NEJM 2005;353:349-361

NEJM 1999;341:1789-1794

DECREASE Study Group

112 patients with a positive dobutamine echo randomized to bisoprolol/placebo started at least a week pre-op and continued for 30-days
Elective vascular surgery
Trial stopped early because of significant differences in nonfatal MI and death from cardiac causes
**Randomized-Prospective Studies**

<table>
<thead>
<tr>
<th>Study</th>
<th>Date</th>
<th>Type of Surgery</th>
<th>Drug</th>
<th>F/U</th>
</tr>
</thead>
<tbody>
<tr>
<td>POBBLE</td>
<td>2005</td>
<td>Vascular</td>
<td>Metoprolol</td>
<td>30 Days</td>
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<td></td>
<td></td>
<td></td>
<td>1 day pre-op</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>to 7 days post-op</td>
<td></td>
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<tr>
<td>DIPOM</td>
<td>2006</td>
<td>Orthopedic, abdominal, Vascular, Neurological, Gynecological</td>
<td>Metoprolol</td>
<td>18 Months</td>
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<td></td>
<td></td>
<td></td>
<td>1 day pre-op until D/C or 6 days post-op</td>
<td></td>
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<tr>
<td>MeV'S</td>
<td>2006</td>
<td>Vascular</td>
<td>Metoprolol</td>
<td>30 Days</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>2 hours pre-op until D/C or 5 days post-op</td>
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<tr>
<td>BBSA</td>
<td>2007</td>
<td>Orthopedic, Urological, Abdominal, Plastic, Gynecological, Vascular</td>
<td>Bisoprolol</td>
<td>30 Days</td>
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<tr>
<td></td>
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<td>3 hours pre-op until D/C or 10 days post-op</td>
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</table>

**THE LANCET**

Effects of extended-release metoprolol or placebo started 24 hours pre-op and continued for 30 days
- 8,349 patients randomized to ER metoprolol/placebo
- Exclusion of all patients on a BB preoperatively
- Vascular, intraperitoneal, orthopedic surgery
- Metoprolol patients had fewer MIs but more deaths and strokes
- Critics felt metoprolol dose too high

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**Meta-analysis of secure randomized controlled trials of β-blockade to prevent perioperative death in non-cardiac surgery**

Sonia Bouri, Matthew James Shun-Shin, Graham D Cole, Jamil Mayet, Darrel P Francis

- In 2011 almost all DECREASE trials found not “secure”
- 9 secure trials totaling 10,529 patients studied
- The study was dominated by POISE data (8,349 pts)
- Perioperative BB caused a 27% risk increase in 30-day mortality
- Revision of cardiology guidelines recommended

**JAMA Surg 2015;150:658-663**

- Retrospective cohort study from 10/2008 - 9/2013
- Use of BB in the window 8-hours prior to admission to 24-hours after admission was determined
- End point was death within 30-days
- Four-point cardiac risk score

**JAMA Surg 2015;150:658-663**

- The risk scores were grouped into 3 categories:
  - No cardiac risk factors
  - 1-2 risk factors
  - 3-4 risk factors
- 326,389 patients after exclusion of percutaneous, endoscopic and cut-down procedures
- Many different types of NCS performed: vascular, orthopedic, abdominal, thoracic, ENT, GYN, urologic, ophthalmologic, plastic, OMFS and neurosurgery

**Cardiac Risk**

<table>
<thead>
<tr>
<th>Lee’s RCRI 1999</th>
<th>Lindemauer 2005</th>
<th>VA Score 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Risk Surgery</td>
<td>High Risk Surgery</td>
<td>Surgery in a Major Body Cavity</td>
</tr>
<tr>
<td>Thoracic</td>
<td>Ischemic Heart Disease</td>
<td>Ischemic Heart Disease</td>
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<tr>
<td>Abdominal</td>
<td>Ischemic Heart Disease</td>
<td>Ischemic Heart Disease</td>
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<td>Suprapelvic</td>
<td>Ischemic Heart Disease</td>
<td>Ischemic Heart Disease</td>
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<tr>
<td>Ischemic Heart Disease</td>
<td>Insulin – Dependent Diabetes</td>
<td>Diabetes</td>
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<tr>
<td>Insulin – Dependent Diabetes</td>
<td>Serum Creatinine</td>
<td>Serum Creatinine</td>
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<td>Serum Creatinine</td>
<td>Serum Creatinine</td>
<td>Serum Creatinine</td>
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<tr>
<td>Cardiogenic Disease</td>
<td>Serum Creatinine</td>
<td>Serum Creatinine</td>
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<tr>
<td>CVA</td>
<td>Serum Creatinine</td>
<td>Serum Creatinine</td>
</tr>
<tr>
<td>Congestive Heart Failure</td>
<td>Cardiacogenic Disease</td>
<td>Cardiacogenic Disease</td>
</tr>
</tbody>
</table>
Odds Ratios and 95% Confidence Intervals for Mortality Associated with the Use of BB in Non-Cardiac Surgery

Conclusions

- BBs appear to be beneficial perioperatively for NCS patients with 3-4 cardiac risk factors.
- The use of BBs in NCS patients with no risk factors should be avoided because of the increased chance of death in this patient cohort.
- Since BB use in NCS patients with 1-2 risk factors did not change the outcome, the use should be seriously questioned. At the very least, patients should be informed of the risk of hypotension and stroke.

Preoperative β-blockers do not improve cardiac outcomes after major elective vascular surgery and may be harmful

- 13,291 patients undergoing LEB, AFB and open AAA
- 8,999 (68%) on a beta blocker (BB):
  - 1,753 (13.2%) started pre-op (<30 days)
  - 7,426 (54.5%) chronic use and were excluded from study
- 4,286 (32.3%) on no BB
- Higher rates of post-op MI with pre-op BB vs. no BB (P=.05) with no difference in 30-day mortality
- Only high-risk open AAA patients on a BB started pre-op had a lower rate of MI (P=.04) than the no BB patients

Association of β-Blocker Therapy With Risks of Adverse Cardiovascular Events and Deaths in Patients With Ischemic Heart Disease Undergoing Noncardiac Surgery: A Danish Nationwide Cohort Study

- 28,263 patients with ischemic heart disease undergoing non-cardiac surgery
- 30-day risk of MACE (ischemic stroke, MI or cardiovascular death) and all-cause mortality
- Beta blocker use was associated with significantly lower risk of 30-day MACE and all-cause mortality only among patients with heart failure (P=.001) or recent MI <2 years (P=.02)

Risk of MACE and all cause mortality with long-term BB therapy in 2 drug combination for uncomplicated hypertensive patients undergoing non-cardiac surgery

- Drugs: BBs, ACE inhibitors, calcium antagonists, thiazides
- 30-day MACE’s in 1.3% of BB patients and 0.8% in non-BB patients (p<.001)
- Results were similar for all-cause mortality
• Few data support the efficacy of pre-op administration of BBs to reduce risk of surgical death
• Consistent and clear associations exist between BB use and adverse outcomes such as bradycardia and death
• These findings are consistent even when DECREASE studies or POISE are excluded

Conclusions
• The "bloom is off the rose" for perioperative BBs
• Patients chronically on BBs should remain on them perioperatively
• Patients should not be started on BBs days or hours prior to surgery (POISE)
• BBs are now second line therapy for hypertension, behind ACE inhibitors and calcium channel blockers:
  ➢ Decreased stroke prevention
  ➢ Danish hypertension study

• BBs may be beneficial in certain "high risk" patients:
  ➢ 3-4 cardiac risk factors
  ➢ Ischemic heart disease with: HF or recent MI (<2 years)
  ➢ Open high risk AAA's
• Ideally, BBs should be started 30-days preoperatively: atenolol, metoprolol or ER metoprolol starting at 25-50mg PO daily and titrating to BP/pulse

References


