

# *Paramedic – Evidence Based Medicine (P-EBP) Program*

## **Paramedic CAT (Critically Appraised Topic) Worksheet**

**Title:** Pre-hospital Administration of Plavix in STEMI + Patients

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**Clinical Scenario:** A 55 year old male patient develops chest pain while playing hockey. The paramedics arrive at the arena, determine the chest pain is ischemic in nature and administer sublingual nitroglycerin, ASA and morphine as per their chest pain protocol. The 12-lead ECG reveals a STEMI. Would the administration of pre-hospital clopidogrel (Plavix) decrease mortality?

### **PICO (Population – Intervention – Comparison – Outcome) Question:**

In the management of prehospital adult ST elevation MI (STEMI), would the addition of clopidogrel (Plavix) to prehospital standard care (Oxygen, ASA, nitroglycerin, and parenteral opioid) compared with standard care alone lead to a decrease in patient mortality?

### **Search Strategy:**

| Search   | Most Recent Queries | Result                |
|--|---------------------|-----------------------|
| <a href="#">#3</a> Search #1 and #2  |                     | <a href="#">35</a>    |
| <a href="#">#2</a> Search Plavix OR clopidogrel  |                     | <a href="#">4600</a>  |
| <a href="#">#1</a> Search paramedic* OR emergency medical technician* OR emergency medical service* OR EMS OR prehospital OR out-of-hospital |                     | <a href="#">39457</a> |

**Search Outcome:** This search yielded 35 papers. Two papers were considered relevant to this PICO question.

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### Relevant Papers:

| Author, Date  | Population:<br>Sample characteristics   | Design<br>(LOE)  | Outcomes   | Results  | Strengths/ Weaknesses  |
|---------------|---|--|--|--|--|
| Sabatine 2005 | A sub-study of the PCI-CLARITY-TIMI 28 trial. Patients with STEMI were randomized on presentation to hospital to receive clopidogrel or placebo in addition to standard treatment with fibrinolysis, ASA, and heparin. All patients underwent mandated coronary angiography within 2 to 8 days. 1862 patients underwent PCI following mandated angiography at which point all received open-label clopidogrel. This study compared patients who received early clopidogrel pre-treatment hours to days before PCI to those who received delayed clopidogrel treatment at the time of PCI. | Prospective randomized double-blind placebo controlled trial | Cardiovascular death, recurrent MI or stroke from PCI to 30 days after randomization   | Pretreatment with clopidogrel led to a significant reduction in the incidence of MI or stroke prior to PCI (4.0% vs. 6.2%), and cardiovascular death or stroke following PCI (3.6% vs. 6.2%). There was no significant increase in incidence of minor or major bleeding events (2.0% vs. 1.9%).  | Not administered in the prehospital setting<br><br>Patients also received fibrinolytic therapy, ASA, and heparin.<br><br>Angiography/PCI not performed for 2-8 days post study drug.<br><br>Does not address CAT question but suggests that earlier administration may lead to improved outcomes   |
| Verheugt 2007 | A pre-hospital sub-study of the CLARITY-TIMI 28 trial. Took place in 11 European ambulance systems where 216 patients (6.2% of the trial cohort of 3491 patients) with STEMI were randomized in the ambulance to clopidogrel (n = 109) or placebo (n = 107) in addition to standard treatment with fibrinolysis, ASA, and heparin.  | Prospective randomized double-blind placebo controlled trial | The composite of an occluded infarct-related artery (TIMI flow grade 0 or 1), or all-cause death, or recurrent MI by predischarge angiography, or day 8, or hospital discharge – whichever came first, for patients who did not undergo angiography.<br><br>30-day incidence of cardiovascular death, recurrent MI or recurrent myocardial ischemia requiring urgent revascularization | The incidence of infarct related artery on the predischarge angiogram was 11.8% in the clopidogrel group vs. 22.3% in the placebo group (trend but not statistically significant).<br><br>There was no reduction in the 30-day incidence of cardiovascular death, recurrent MI or recurrent myocardial ischemia requiring urgent revascularization.<br><br>There was no increase in severe bleeding in those treated with prehospital clopidogrel. | Small sample size (n= 216)<br><br>All patients received prehospital fibrinolytic therapy, ASA, and heparin in addition to study drug.<br><br>Not equivalent to current Canadian prehospital care of STEMI.<br><br>Does not directly address the CAT question but suggests that prehospital administration may lead to improved outcomes. |

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### **Comments:**

These two studies seem to indicate that early administration of clopidogrel as part of an STEMI management strategy that includes thrombolysis, ASA, and heparin results in greater coronary artery patency compared to placebo, without an apparent increase in bleeding complications. The second study demonstrates a trend towards improved coronary patency when clopidogrel is administered in the prehospital setting. In both studies the standard care included fibrinolytics therapy and heparin, which is not the standard care in most Canadian EMS systems and may not be the primary treatment modality in urban hospital facilities.

### **Clinical Bottom Line:**

Clinical benefit of prehospital administration of clopidogrel in addition to standard care consisting of only ASA, oxygen, and parenteral opioid administration remains to be established. A large prospective, randomized placebo controlled trial comparing the addition of clopidogrel to Canadian prehospital STEMI care vs. standard care is required.

### **References:**

Verheugt F, et al. Prehospital fibrinolysis with dual antiplatelet therapy in ST-elevation acute myocardial infarction: a sub study of the randomized double blind CLARITY-TIMI 28 trial. *J Thromb Thrombolysis* 2007;23: 173-179.

Sabatine MS, et al. Effect of Clopidogrel pretreatment before percutaneous coronary intervention in patients with ST-elevation myocardial infarction treated with fibrinolytics. *JAMA* 2005; 294: 1224-1232.