

Paramedic - Evidence Based Medicine (P-EBP) Program

Paramedic CAT (Critically Appraised Topic) Worksheet

Title: *Early prehospital administration of P2Y12 inhibitor Ticagrelor to STEMI patients*

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2nd Party Appraiser: *Jen Greene*

Clinical Scenario: *With the high prevalence of CAD and the clinical significance of STEMI events, we were interested in exploring early antiplatelet therapy and finding out if it could improve patients' clinical outcomes.*

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

In patients diagnosed with a STEMI does the prehospital administration of Ticagrelor antiplatelet therapy impact infarct size or TIMI flow?

Search Strategy:

("emergency medical services"[MeSH Terms] OR ("emergency"[All Fields] AND "medical"[All Fields] AND "services"[All Fields]) OR "emergency medical services"[All Fields] OR ("emergency medical technicians"[MeSH Terms] OR ("emergency"[All Fields] AND "medical"[All Fields] AND "technicians"[All Fields]) OR "emergency medical technicians"[All Fields]) OR "paramedic*"[All Fields] OR (("emerge"[All Fields] OR "emerged"[All Fields] OR "emergence"[All Fields] OR "emergences"[All Fields] OR "emergencies"[MeSH Terms] OR "emergencies"[All Fields] OR "emergency"[All Fields] OR "emergent"[All Fields] OR "emergently"[All Fields] OR "emergents"[All Fields] OR "emerges"[All Fields] OR "emerging"[All Fields]) AND ("medic"[All Fields] OR "medical"[All Fields] OR "medicalization"[MeSH Terms] OR "medicalization"[All Fields] OR "medicalizations"[All Fields] OR "medicalize"[All Fields] OR "medicalized"[All Fields] OR "medicalizes"[All Fields] OR "medicalizing"[All Fields] OR "medically"[All Fields] OR "medicals"[All Fields] OR "medicated"[All Fields] OR "medication s"[All Fields] OR "medics"[All Fields] OR "pharmaceutical preparations"[MeSH Terms] OR ("pharmaceutical"[All Fields] AND "preparations"[All Fields]) OR "pharmaceutical preparations"[All Fields] OR "medication"[All Fields] OR "medications"[All Fields]) AND "technician*"[All Fields]) OR ("prehospital"[All Fields] OR "prehospitally"[All Fields]) OR "pre-hospital"[All Fields] OR "out of hospital"[All Fields] OR "responder*"[All Fields] OR ("ambulance s"[All Fields] OR "ambulances"[MeSH Terms] OR "ambulances"[All Fields] OR "ambulance"[All Fields])) AND ("st elevation myocardial infarction"[MeSH Terms] OR ("st"[All



Paramedic - Evidence Based Medicine (P-EBP) Program

Fields] AND "elevation"[All Fields] AND "myocardial"[All Fields] AND "infarction"[All Fields]) OR "st elevation myocardial infarction"[All Fields] OR "stemi"[All Fields] OR "stemis"[All Fields] OR "OMI"[All Fields] OR ("myocardial infarction"[MeSH Terms] OR ("myocardial"[All Fields] AND "infarction"[All Fields]) OR "myocardial infarction"[All Fields]) OR ("ann cardiothorac surg"[Journal] OR "adv comm swallowing"[Journal] OR "acs"[All Fields]) OR "acute coronary syndrome"[All Fields]) AND ("aspirin"[MeSH Terms] OR "aspirin"[All Fields] OR "aspirins"[All Fields] OR "aspirin s"[All Fields] OR "aspirine"[All Fields] OR ("anal sci adv"[Journal] OR "asa"[All Fields]) OR ("aspirin"[MeSH Terms] OR "aspirin"[All Fields] OR ("acetylsalicylic"[All Fields] AND "acid"[All Fields]) OR "acetylsalicylic acid"[All Fields])) AND ("clopidogrel"[MeSH Terms] OR "clopidogrel"[All Fields] OR "plavix"[All Fields] OR "clopidogrel s"[All Fields] OR ("ticagrelor"[MeSH Terms] OR "ticagrelor"[All Fields]) OR "P2Y12"[All Fields] OR ("clopidogrel"[MeSH Terms] OR "clopidogrel"[All Fields] OR "clopidogrel s"[All Fields]) OR "dual antiplatelet therapy"[All Fields] OR ("anticoagulants"[Pharmacological Action] OR "anticoagulants"[MeSH Terms] OR "anticoagulants"[All Fields] OR "anticoagulant"[All Fields] OR "anticoagulate"[All Fields] OR "anticoagulated"[All Fields] OR "anticoagulating"[All Fields] OR "anticoagulation"[All Fields] OR "anticoagulations"[All Fields] OR "anticoagulative"[All Fields]))

Search Outcome:

249

Relevant Papers:

AUTHOR, DATE	POPULATION: SAMPLE CHARACTERISTICS	DESIGN (LOE)	OUTCOMES	RESULTS	STRENGTHS/ WEAKNESSES
Montalescot et al., 2014	1875 patients diagnosed with STEMI	Double Blind Randomized Control Trial	Resolution of ST-segment elevation $\geq 70\%$ before PCI TIMI flow Gr3 in infarct-related artery before PCI	<u>Resolution of ST-segment elevation $\geq 70\%$ before PCI:</u> 87.6% in the control group vs 86.8% in the intervention group (p=0.63) <u>TIMI flow Gr3 in infarct-related artery before PCI:</u> 83.1% in the control group vs 82.6% in the intervention group (p=0.82)	Strengths: - Study design (double-blind RCT) - Partly done in Canada (as far as translating findings to our operations) Weaknesses: - Combination of short transport times + pharmacokinetics of specific drug used may



Paramedic - Evidence Based Medicine (P-EBP) Program

					have negatively impacted results - Small sample size
d'Entremont et al., 2020	<p>709 patients diagnosed with STEMI</p> <ul style="list-style-type: none"> - 482 patients in earlier intervention group received ASA + ticagrelor + heparin before transfer to PCI centre <p>227 patients in the later intervention group received in-ambulance ASA, followed by ticagrelor + heparin @ PCI centre.</p>	Retrospective cohort study	<p>Primary outcome:</p> <ul style="list-style-type: none"> - The presence of a pre-PPCI TIMI flow 2-3 in the infarct related artery (IRA). <p>Secondary Outcome: - Acute definite stent thrombosis</p> <ul style="list-style-type: none"> - Hemorrhagic complications. 	<p><u>Primary outcome:</u> 44.6% Reached TIMI Flow Gr 2-3 in earlier intervention group vs 18.5% in the later group (p<0.0001)</p> <p><u>Secondary outcomes:</u> 0.6% had acute definite stent thrombosis in the earlier intervention group vs 2.6% in the later group (p=0.03)</p> <p>1.9% had adverse bleeding events in the earlier intervention group vs 3.5% in the later group (p=0.18)</p>	<p>Strengths:</p> <ul style="list-style-type: none"> - Strong external validity. - Empirical data - Relatively large sample for this type of study <p>Weaknesses:</p> <ul style="list-style-type: none"> - Single-center - Cohorts were not identical - Different medication formats used (crushed vs integral tablets) and data was not collected - Data regarding symptom onset to reperfusion not available

Comments: Both studies had Canadian involvement. This was useful for contextually translating results into our operations but it was not an intentional part of our search.

Consider: Studies have so far failed to conclusively show a benefit from early ticagrelor administration to patients with STEMI going for PCI. However, short transport times to Cath labs as well as unfavourable ticagrelor pharmacokinetics have emerged as possible hypotheses to explain the lack of results from the ATLANTIC study, as well as other similar research.

The addition of unfractionated heparin (UFH) to pre-PPCI antiplatelet therapy and the possible synergistic effect between UFH and Ticagrelor is interesting, however more Level I research is needed that better controls groups and interventions.



Paramedic - Evidence Based Medicine (P-EBP) Program

Clinical Bottom Line: There is currently insufficient evidence to support routine prehospital administration of ticagrelor \mp heparin to STEMI patients, but research has identified possible benefits in certain situations with few adverse effects. Development of newer antiplatelet therapies with more favourable pharmacokinetics for prehospital use is an intriguing area that should be explored.

References:

d'Entremont, M., Laferrière, C., Bérubé, S., Couture, É. L., Lepage, S., Huynh, T., Verreault-Julien, L., Karzon, A., Desgagnés, N., & Nguyen, M. (2020). The effect of ASA, ticagrelor, and heparin in ST-segment myocardial infarction patients with prolonged transport times to primary percutaneous intervention. *Catheterization and Cardiovascular Interventions*, 97(4), 591–599. <https://doi.org/10.1002/ccd.29144>

Montalescot, G., van 't Hof, A. W., Lapostolle, F., Silvain, J., Lassen, J. F., Bolognese, L., Cantor, W. J., Cequier, Á., Chettibi, M., Goodman, S. G., Hammett, C. J., Huber, K., Janzon, M., Merkely, B., Storey, R. F., Zeymer, U., Stibbe, O., Ecollan, P., Heutz, W. M. J. M., & Swahn, E. (2014). Prehospital ticagrelor in ST-segment elevation myocardial infarction. *New England Journal of Medicine*, 371(11), 1016–1027. <https://doi.org/10.1056/nejmoa1407024>

