プライマリPCIにおけるヘパリンを超えるエノキサパリンの支持

ATOLL：プライマリPCIにおいてエノキサパリン静脈内投与の虚血に関する予後は未分画ヘパリン投与よりも良好である

ATOLL: Intravenous enoxaparin associated with better ischemic outcomes in primary PCI than unfractionated heparin

ST上昇MIに対するプライマリPCIにおいて2種類の抗凝固療法を比較したATOLLトライアルの結果、低分子ヘパリンであるエノキサパリンはこのような症例において従来使用されている未分画ヘパリンよりも予後を改善する可能性があると2010年European Society of Cardiology学会で発表された。Phase III ATOLLトライアルは910人の患者（75歳以上18%、5%がショックまたは心停止）をエノキサパリン静脈内投与（抗血小板療法としてのGP IIb/IIIa受容体阻害薬併用の有無にかかわらず0.5mg/kg、および凝固能モニターなし）または未分画ヘパリン静脈内投与（GP IIb/IIIa受容体阻害薬併用時50～70IU/kg、GP IIb/IIIa受容体阻害薬非併用時70～100IU、抗凝固モニターにより用量調節）を冠動脈造影前に施行した。一次エンドポイント（30日間の死亡、MI合併症、PCI不成功またはCABG以外による重大な出血の合計）はエノキサパリンにより34%から28%に減少した（RR 17%）が、統計学的な有意差には到達しなかった（P=0.07）。主要な二次エンドポイント（死亡、MI/ACS再発または緊急血行再建術から成る虚血エンドポイントの合計）は11.3%から6.7%と、41%減少した（P=0.02）。死亡、再梗塞または緊急血行再建術の古典的な3つのエンドポイントは8.5%から5.1%に減少した（P=0.04）。エノキサパリンにより死亡またはMI合併症が12.4%から7.8%に減少した（RR 37%、P=0.02）。総死亡は6.3%から3.8%に減少し、死亡または蘇生された心停止は7%から4%に減少した（P=0.05）。

Full Text

Results from ATOLL, a phase 3 randomized trial comparing two anticoagulants in primary PCI for ST elevation MI, show that the low molecular weight heparin enoxaparin may provide better outcomes in such cases than the traditionally used unfractionated heparin. The study was presented during a Hotline session at the European Society of Cardiology Congress 2010.

The former, explained principal investigator Professor Gilles Montalescot from the Cardiology Department of Piti?-Salp?tri?re University Hospital, Paris, has already been associated with a 57% relative risk reduction of major bleeding when compared with unfractionated heparin (UFH) in a large randomized study performed in elective PCI. But so far, primary PCI for STEMI has traditionally been supported by unfractionated heparin. The aim of the ATOLL study was to compare head-to-head intravenous enoxaparin with UFH in patients undergoing PCI for STEMI. "The time has come to acknowledge that there is better anticoagulation than UFH in PCI, primary PCI included," said Professor Montalescot.

ATOLL was a 43-site multicentre randomized trial in STEMI patients scheduled for primary PCI. Randomization mostly occurred before hospital admission. The primary endpoint was the composite of death, complications of MI, procedure failure or non-CABG major bleeding at 30 days. The main secondary endpoint was the ischemic composite endpoint of death, recurrent MI/ACS or urgent revascularization. Death or complications of MI was also examined, while the main safety endpoint was major bleeding (according to the STEEPLE definition) during hospital stay. The net clinical benefit combined death, complications of MI or major bleeding.

At 43 sites in four countries (Austria, France, Germany, USA), 910 patients were randomized to receive IV enoxaparin (0.5mg/kg, same dose with or without glycoprotein IIb/IIIa inhibitors as antiplatelet therapy, and no coagulation monitoring) or IV UFH (50-70IU/kg with GPIIb/IIIa inhibitors, 70-100IU without GPIIb/IIIa inhibitors, and dose adjusted to anti-coagulation monitoring) before coronary angiography. Patients were excluded if they had received any anticoagulant before randomization, so that patients were uniformly treated with one or the other anticoagulant. The technical aspects of the PCI - including type of arterial access, stenting, choice of stents as well as use of intra-aortic balloon pumps - were left to the discretion of the investigators, said Professor Montalescot.

Results from the study showed that a high-risk population was recruited, 18% of them elderly (over 75 years) and 5% in shock or cardiac arrest. Primary PCI was performed through a radial access in 68% of cases, with 75% of patients receiving GPIIb/IIIa inhibitors and two-thirds of patients receiving high dose clopidogrel.

The primary endpoint was reduced with enoxaparin from 34% to 28% (RR 17%), but did not reach statistical significance (p=0.07). The main secondary endpoint was significantly reduced by 41%, from 11.3% to 6.7% (p=0.02). The classic triple ischemic endpoint of death, reinfarction or urgent revascularization was also reduced from 8.5% to 5.1% (p=0.04). Enoxaparin reduced the endpoint of death or complications of MI from 12.4% to 7.8% (RR 37%, p=0.02). Death (any cause) decreased from 6.3% to 3.8% (p=0.08) and death or resuscitated cardiac arrest decreased from 7% to 4% with enoxaparin (p=0.05).

The main safety endpoint occurred in 4.9% of patient on enoxaparin and 4.5% of patients on UFH (non-significant), translating into a superiority of enoxaparin over UFH for a net clinical benefit (of death, complication of MI or major bleeding) of 15% vs. 10.2% (p=0.03).

Commenting on the results, Professor Montalescot said: "We have performed the first pure head-to-head comparison between two anticoagulants in primary PCI, with all antiplatelet agents being even. In this comparison, IV enoxaparin did not reduce procedural failure, in particular low TIMI flow and non ST-resolution, which had a direct impact on the primary endpoint. However, harder ischemic endpoints were all reduced with IV enoxaparin on top of intense antiplatelet therapy.

"Enoxaparin also showed a good safety profile with a superior net clinical benefit. Our data demonstrate that this strategy, which is easier to use, is also more effective at reducing the most serious ischemic complications of STEMI treated with primary PCI."

Conference News