Anti-Inflammatory Treatment With Colchicine in Acute Myocardial Infarction: A Pilot Study

Running title: Deftereos et al.; Colchicine in STEMI

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Abstract

**Background**—Inflammatory processes have been identified as key mediators of the deleterious effects of ischemia/reperfusion in ST-elevation myocardial infarction (STEMI). Colchicine is a substance with potent anti-inflammatory properties, suitable for safe use in patients with cardiovascular disease. The purpose of this study was to test the hypothesis that a short course of colchicine treatment could lead to reduced infarct size.

**Methods and Results**—Patients presenting with STEMI 12 hours or less from pain onset (treated with primary percutaneous coronary intervention) were randomized to colchicine or placebo for 5 days. The primary outcome parameter was the area under the curve of creatine kinase-MB (CK-MB) concentration. A subset of patients underwent cardiac magnetic resonance imaging (MRI) with late gadolinium enhancement (LGE) 6-9 days after the index STEMI. 151 patients were included (60 in the MRI substudy). The area under the CK-MB curve was 3144 [IQR 1754-6940] ng.h.ml⁻¹ in the colchicine group as compared to 6184 [IQR 4456-6980] ng.h.ml⁻¹ in controls (p<0.001). Indexed MRI-LGE-defined infarct size was 18.3 [IQR 7.6-29.9] ml/1.73 m² in the colchicine group versus 23.2 [18.5-33.4] ml/1.73 m² in controls (p=0.019). The relative infarct size (as a proportion to left ventricular myocardial volume) was 13.0 [IQR 8.0-25.3]% and 19.8 [IQR 13.7-29.8]%, respectively (p=0.034).

**Conclusions**—These results suggest a potential benefit of colchicine in STEMI, but further clinical trials are necessary to draw secure conclusions, especially considering the fact that the present study was not powered to assess clinical endpoints

**Clinical Trial Registration Information**—clinicaltrials.gov. Identifier: NCT01936285.

**Key words:** creatine kinase, magnetic resonance, late gadolinium enhancement, infarct size, troponin T
Introduction

Over the last years, a substantial volume of evidence has accumulated identifying inflammatory processes as key mediators of the deleterious effects of ischemia/reperfusion-related phenomena in patients presenting with ST-elevation myocardial infarction (STEMI).\(^1\)\(^-\)\(^4\) Nevertheless, equally impressive is the lack of clinically applicable therapeutic strategies that could mitigate these processes, thus providing significant cardioprotection.

Despite the well-known fact that inflammation plays an important role in coronary artery disease development and progression,\(^5\)\(^-\)\(^6\) there have been few attempts to systematically examine the potential role of anti-inflammatory treatment in this setting, possibly due to a lack in anti-inflammatory agents without the adverse cardiovascular safety profile of corticosteroids and nonsteroidal anti-inflammatory drugs.\(^7\)\(^-\)\(^9\) Colchicine is a substance with potent anti-inflammatory properties, having a unique mechanism of action, which allows for safe use in patients with cardiovascular disease.\(^10\)

The purpose of the present clinical study was to test the hypothesis that a short course of treatment with colchicine could lead to reduced infarct size in patients presenting with STEMI and treated with primary percutaneous coronary intervention (PCI).

Methods

This was a prospective, double-blinded, placebo-controlled study, performed in two primary PCI referral hospitals in the greater Athens area, while magnetic resonance imaging (MRI) studies were all performed in a third (separate) center. Patients presenting with STEMI, 12 hours or less from the onset of chest pain, from July 2013 until March 2015, were included. Main exclusion criteria were: age \(\leq 18\) or \(\geq 80\) years, active inflammatory or infectious disease or known
malignancy, current treatment with corticosteroids or other anti-inflammatory agents, known hypersensitivity to colchicine or current chronic treatment with colchicine, severe renal failure (estimated glomerular filtration rate <30 ml/min/1.73 m²), hepatic failure (Child - Pugh class B or C), cardiac arrest, ventricular fibrillation or cardiogenic shock as presenting symptom, stent thrombosis, angina within 48 hours before infarction, previous myocardial infarction, occlusion of the left main or left circumflex coronary artery or with evidence of coronary collaterals to the region at risk on initial coronary angiography, presence of metallic implants (ferromagnetic material), inability or unwillingness to provide informed consent. The protocol was approved by the institutional review boards and was implemented in accordance with the provisions of the Declaration of Helsinki. All patients provided informed consent.

After completion of the diagnostic coronary angiography, patients were randomized (using a 1:1 allocation scheme based on a computer-generated randomization algorithm – an R language script was used for this purpose) to receive colchicine, starting with a loading dose of 2 mg (1.5 mg initially followed by 0.5 mg one hour later) and continuing with 0.5 mg twice daily, or placebo, for 5 days (Figure 1). Patients with less than 60-kg body weight received 0.5 mg once daily. Monitoring of adverse events focused on gastrointestinal manifestations, hepatotoxicity, myelotoxicity and myotoxicity. Operators and personnel involved in patient follow-up and management were blinded as to patient allocation (patient treatment was identified by a serial number; assignment records were kept in a digital file which was unlocked after conclusion of last patient follow-up procedures and database locking).

All patients received standard-of-care treatment for STEMI. During primary PCI, bivalirudin, heparin and/or glycoprotein IIb/IIIa inhibitors were used at the discretion of the treating interventionalist. Standard medical therapy was administered, including beta-blockers,
statins, acetyl-salicylic acid and ticagrelor or prasugrel at recommended daily dosages.

The primary outcome parameter was the area under the curve of creatine kinase-myocardial brain fraction (CK-MB) concentration over 72 hours after admission (calculated using the Simpson’s summing rule\(^{11}\)). CK-MB was measured on admission and every 4 hours thereafter. Maximal high-sensitivity troponin T (hs-TnT) was a secondary outcome measure over the same time period. A subset of patients from the total cohort underwent cardiac MRI with late gadolinium enhancement (LGE) 6-9 days after the index STEMI (MRI subgroup). In this subgroup, absolute myocardial infarct volume, determined by LGE, was the primary outcome measure. Myocardial infarct volume indexed to body-surface area and relative infarct size (proportion of absolute infarct volume to left ventricular myocardial volume) were secondary outcome measures.

Blood samples for hs-TnT (Elecsys Troponin T hs assay, Roche Diagnostics; lower detection limit 5 pg/ml) and CK-MB (Elecsys CK-MB assay, Roche Diagnostics; lower detection limit <0.1 ng/ml) measurement, as well as other analyses (complete blood count, biochemistries, including high-sensitivity C-reactive protein [CRP] etc.) were obtained at baseline (on admission), every 4 hours for the first 72 hours post-presentation, and every 12 hours thereafter. All patients had a standard transthoracic echocardiographic study performed before discharge, whereupon left ventricular ejection fraction was calculated with the modified Simpson’s rule.

**Cardiac MRI**

The cardiac MRI protocol was performed on a 1.5T Siemens Symphony system (Erlangen, Germany). Approximately 8-9 minutes after administration of 0.015-0.02 mmol/kg of gadobutrol (Gadovist®, Bayer Hellas AG), a multi-phase inversion-recovery steady state free precession
(SSFP) scan (“TI-scout”) was acquired in the mid short-axis plane, in order to determine the optimal inversion time (TI) to null normal myocardium for delayed enhancement imaging. The time that corresponded to the image with sufficiently nulled myocardium was inputted as the TI into the subsequent inversion recovery segmented turbo flash sequence used for delayed enhancement imaging. Typically, the TI spanned 230-330 ms over the course of the study. Other imaging parameters were: TR/TE/flip = 700ms/4.18ms/25deg, 8 mm thickness, field of view = 255x340 mm, 192x256, and 25 segments. Acquisition was performed in the short-axis, covering the left ventricle from base to apex. In addition, single slices were acquired in the long-axis, four chamber and three chamber views. The TI was increased as needed as time passed (10-20 minutes after gadobutrol administration). In order to quantify myocardial scar short-axis delayed enhancement images were analyzed using the freely available for research purposes software Segment, version 1.9 R2354 (http://segment.heiberg.se) (Figure 2).  

Sample size estimation and statistical analysis  
Preliminary measurements in patients presenting with STEMI at our institution had an area under the CK-MB concentration curve in the first 72 hours of approximately 6000 units [(ng/ml)*h] with a standard deviation of approximately 3000 units. It was calculated that in order to detect a 25% reduction in the primary outcome measure with 85% probability (type II error probability 0.15), at an alpha level (Type I error probability) of 0.05, 150 subjects would have to be included. Analysis was performed on an intention-to-treat basis (all randomized patients). Continuous variables were expressed as median [25th-75th percentile]. Comparisons of central tendencies and correlations were tested using non-parametric tests (Mann-Whitney U and Spearman, respectively). Categorical variables were expressed as counts and percentages and compared using the $\chi^2$ test (or Fisher exact test, if the generated 2x2 contingency tables contained
cells with expected counts equal or less than 5). SPSS 17 software package (SPSS Inc., Chicago, IL, USA) and R language were used for all analyses. \( p \) values less than 0.05 (two-sided) were considered as indicative of statistical significance.

**Results**

151 patients (104 male) were included in the final analysis (77 in the colchicine group and 74 controls). 60 (41 male) of these patients were included in the MRI substudy. The epidemiological and clinical characteristics of the two cohorts (as a whole and divided in the two treatment arms) are summarized in Table 1. The two treatment arms were similar in respect to important baseline parameters, both in the whole cohort (the only notable trend was a non-significantly higher thrombus burden in the colchicine arm) and the MRI subgroup. The MRI subgroup characteristics did not differ in any significant way from those of the total cohort.

**Total cohort**

The median number of CK-MB measurements per patient was 16 [15-16] (without any significant difference between treatment groups; \( p=0.226 \)). The area under the curve of CK-MB concentration was 3144 [1754-6940] ng.h.ml\(^{-1}\) in the colchicine group as compared to 6184 [4456-6980] ng.h.ml\(^{-1}\) in patients who took placebo (\( p<0.001 \); Figure 3). A similar difference was observed in maximum troponin values: median maximum hsTnT was 19763 [6692-51922] pg/ml and 45550 [19706-75556] pg/ml in the colchicine and control arms, respectively (\( p=0.001 \)), although one cannot fail to note the marked dispersion of values in the colchicine group, also obvious in the area-under-the-CK-MB-curve boxplot graph (Figure 3). The pre-discharge echocardiographic left ventricular ejection fraction was 53 [44-59] \% in the colchicine group versus 46 [38-51] \% in controls (\( p=0.003 \)).
MRI subgroup

MRI-LGE-defined infarct size, both in terms of absolute infarct volume and relative infarct size (proportion of infarct to left ventricular myocardial volume) was smaller in colchicine-treated individuals (Figure 4). Absolute infarct volume was 25.1 [20.0-35.9] ml in controls as opposed to 18.8 [8.1-28.5] ml in the colchicine group (p=0.019). After normalization for body-surface area, the corresponding indexed infarct sizes were 23.2 [18.5-33.4] ml/1.73 m² versus 18.3 [7.6-29.9] ml/1.73 m² (p=0.019). The relative infarct size was 19.8 [13.7-29.8] % and 13.0 [8.0-25.3] %, respectively (Figure 4). Biomarker-defined infarct size was also lower in colchicine-treated patients of the MRI subset, similarly to the total cohort (Figure 4). Expectedly, there was a significant correlation between MRI- and biomarker-defined infarct size, which suggests good internal consistency of the data (Figure 5A).

Study treatment discontinuation and adverse effects

Overall, 23 of 151 patients discontinued treatment before taking all study drug doses. Discontinuation rate was 26% percent in the colchicine group (20 of 77 patients), as opposed to 4% in the control group (3 of 74 patients) (p<0.001). The reason for discontinuing the study drug was reported as “diarrhea” in 16 of 23 cases (15 belonged to the colchicine group and 1 to the control group) and “nausea/vomiting” in 3 cases (all in the colchicine group). In one case, marked elevation in serum alanine aminotransferase was reported as the reason for study drug discontinuation (up to approximately 5 times the upper reference limit, without any sequelae).

No cases of myelotoxicity were reported. In-hospital death occurred in 1 patient of the colchicine group and 1 of the control group (on days 4 and 5 of hospitalization, respectively).

The area under the curve of CK-MB concentration was 2312 [1201-5743] ng.h.ml⁻¹ in patients of the colchicine group who completed treatment (N=57) versus 5920 [2998-8858]
ng.h.ml\(^{-1}\) in those who stopped treatment (N=20) (p=0.003). The corresponding values for absolute infarct size in the MRI subgroup were 12.4 [6.8-25.9] ml in patients who completed colchicine treatment (N=24) versus 29.1 [26.1-36.6] ml in those who discontinued (N=7) (p=0.008).

**Inflammatory markers**

Maximal neutrophil count (the highest neutrophil count measured during hospitalization) was 7543 [6549-10118] /µL in the colchicine group compared to 8922 [7880-10307] /µL in controls (p=0.008). It was significantly associated with relative and absolute MRI-LGE infarct size (Figure 5B), as well as with the area under the CK-MB curve (Spearman’s rho 0.79; p<0.001). These correlations were significant independently of study treatment (colchicine or placebo).

Maximal CRP levels were also higher in the control group compared with colchicine-treated patients (63.8 [34.7-103.4] mg/l versus 42.9 [16.3-71.4] mg/l; p=0.019). Maximal CRP was correlated (although less strongly than neutrophil count) with relative MRI-LGE infarct size (Spearman’s rho 0.42; p=0.001), indexed absolute infarct size (Spearman’s rho 0.43; p=0.001) and the area under the CK-MB curve (Spearman’s rho 0.38; p<0.001).

**Discussion**

The results of this prospective randomized study indicate that treatment with colchicine in patients with STEMI undergoing primary PCI is associated with smaller infarct size, as defined by both biomarker release and MRI-LGE. This effect was accompanied by a substantial treatment-related difference in markers of post-myocardial-infarction inflammatory response, namely neutrophil count and C-reactive protein. These latter parameters were quite strongly associated with infarct size.
Inflammation has been shown to be implicated in several processes involved in the sequence of events that follow the obstruction of an epicardial coronary artery in the context of STEMI, including thrombus composition,\textsuperscript{13} endothelial function,\textsuperscript{14,15} post-infarction myocardial function,\textsuperscript{16,17} clinical events,\textsuperscript{18-22} and, even, peri-infarct kidney injury.\textsuperscript{23} There is also evidence that timelier reperfusion leads to a blunted inflammatory response,\textsuperscript{24} while C-reactive protein levels following STEMI are predictive of left ventricular remodeling\textsuperscript{25} and inflammatory mediators are correlated with biomarkers of cardiac dysfunction.\textsuperscript{26} Most importantly, specific components of the cellular inflammatory response have been shown to be strongly correlated with STEMI-related myocardial damage: monocyte response has been associated with severe myocardial injury and poor functional outcome after STEMI\textsuperscript{27} and neutrophil peaks have been found to predict MRI-defined infarct size.\textsuperscript{28} In view of this evidence, the significant inverse correlation of colchicine treatment with post-STEMI neutrophil rise, which was observed in the present study, suggests a potential mechanism of the observed beneficial effect of colchicine (along with the observed association of neutrophil count with infarct size, which was strong for all patients independently of treatment allocation).

Colchicine is a drug with well-known anti-inflammatory properties, shown to be safe in various settings of cardiovascular disease.\textsuperscript{29-31} Its unique effects stem from its ability to interfere with microtubule polymerization. At a structural level, each hollow microtubule is assembled from 13 parallel protofilaments, which in turn are comprised of alternating, very tightly linked, \(\alpha\)- and \(\beta\)-tubulin subunit pairs organized along a longitudinal axis.\textsuperscript{32} Colchicine binds to the intradimeric \(\alpha\)-\(\beta\) interface, in the center of the tubulin heterodimer.\textsuperscript{33-35} By interfering with microtubule polymerization, colchicine affects virtually every process that requires cytoskeletal changes, including cell mitosis, exocytosis and motility and, mainly due to its pharmacokinetics,
these effects are particularly potent on inflammatory cells.\textsuperscript{36} Inhibition of interleukin-1 production by activated neutrophils, down-regulation of tumor necrosis factor alpha-receptors in macrophages and endothelial cells, and impairment of the adhesion of neutrophils to the vascular endothelium, probably through modulation of endothelial E-selectin and neutrophil L-selectin surface expression are some of the ways colchicine affects inflammatory responses.\textsuperscript{36,37} Experimental or clinical data regarding the role of colchicine in STEMI are sparse. In one study, in an open-chest canine model of reperfusion injury, the number of circulating neutrophils, neutrophil cytotoxicity, and neutrophil myocardial accumulation after 6 hours of reperfusion were reduced in colchicine-treated dogs, although there was no difference in infarct size.\textsuperscript{38} To our knowledge, no study has assessed the effect of colchicine on infarct size in humans. Raju et al.\textsuperscript{39} studied a mixed population of 80 patients with STEMI, non-ST-elevation acute coronary syndrome and ischemic stroke and found no difference in C-reactive protein between patients on colchicine and controls 30 days after the index event (a time point one would expect acute inflammatory processes to have subsided even in patients not taking any anti-inflammatory treatment, which renders this finding difficult to interpret in a clinically meaningful way). On the other hand, colchicine has already been shown to be associated with reduced myocardial damage in another setting of ischemia/reperfusion myocardial insult, namely that of cardiac surgery.\textsuperscript{40}

Studies of other agents with anti-inflammatory action have given varying results in improving outcomes following STEMI. In two small studies, an interleukin-1 inhibitor was associated with lower incidence of heart failure after the index myocardial infarction.\textsuperscript{41,42} However, in another study in non-ST-elevation acute coronary syndrome patients, the same agent, despite a significant reduction in biomarkers of inflammation, was associated with more recurrent events at 1 year (although it should be noted that this study was not designed to
evaluate clinical endpoints and, in any case, non-ST elevation acute coronary syndrome
pathophysiology differs substantially from that of STEMI). Of note, the immunosuppressive
agent cyclosporine has been shown to have a beneficial effect on infarct size in STEMI; although the authors suggest that cyclosporine had a cardioprotective effect due to inhibition of
the opening of mitochondrial permeability-transition pores, the possibility that its
immunosuppressive action may also have played a role in the observed effect cannot be
discounted. In any case, interest in this area of research remains unabated, with large clinical
trials of novel anti-inflammatory agents under way.

In this context, the findings of the present study are quite remarkable, given that a
favorite effect of treatment was found in all studied parameters (biomarkers and cardiac MRI). It
is possible that the broadness of colchicine effects (affecting various pathways of the
inflammatory processes) is an advantage in the complex pathophysiologic interplay between
inflammation, ischemia and reperfusion in reperfused STEMI. However, one should probably go
beyond statistical significances and note, by observing the distribution of evaluated infarct sizes
in colchicine-treated patients (for example in Figure 3), that there was a marked dispersion of
values, possibly indicating considerable heterogeneity in the drug effect (or, even more probably,
a result of the considerable proportion of premature discontinuation of the study drug). This
observation, along with the fact that the study was not powered to demonstrate differences in
hard clinical endpoints, must define the boundaries in generalizing these results: they are
certainly compelling, pointing towards potential usefulness of colchicine in this setting, but
further studies are definitely necessary to draw secure clinical conclusions.

Study limitations

The studied measures of infarct size (CK-MB output and MRI-LGE infarct size) are well-
validated in this setting, with good correlation with prognosis\textsuperscript{46,47} although limitations can arise both in the case of CK-MB (for example when different sampling intervals are used in the concentration versus time plot and when comparing patients with altered enzyme kinetics) and in the case of MRI (probably the most important factor is the timing of the measurement relative to the index event). These potential sources of error were carefully kept to a minimum in the present study.

**Funding Sources:** This was an investigator-initiated and -funded study.

**Conflict of Interest Disclosures:** None.

**References:**


### Table 1. Demographic, clinical and procedural patient characteristics per randomization group.

<table>
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<th>Variable</th>
<th>Total (N=151)</th>
<th>MRI subset (N=60)</th>
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<td></td>
<td>Control (N=74)</td>
<td>Colchicine (N=77)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>58 [51-68]</td>
<td>58 [52-64]</td>
</tr>
<tr>
<td>Male gender</td>
<td>52 (70%)</td>
<td>52 (68%)</td>
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<td>Body mass index (kg/m²)</td>
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<td>27.1 [25.3-30.7]</td>
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<tr>
<td>Body surface area (m²)</td>
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<td>eGFR (ml/min/1.73 m²)</td>
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<td>75 [55-100]</td>
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<td>Smoking</td>
<td>36 (49%)</td>
<td>43 (56%)</td>
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<td>Diabetes mellitus</td>
<td>19 (26%)</td>
<td>13 (17%)</td>
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<tr>
<td>Hypertension</td>
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<td>31 (40%)</td>
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<td>Ischemia time (min)</td>
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<td>173 [141-223]</td>
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<td>Baseline hsTnT (pg/ml)</td>
<td>34 [8-304]</td>
<td>37 [9-361]</td>
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<td>Baseline CK-MB (µg/ml)</td>
<td>44 [35-71]</td>
<td>59 [33-74]</td>
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<td>Baseline neutrophil count (/µl)</td>
<td>7131 [5913-7950]</td>
<td>6947 [5929-8935]</td>
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<tr>
<td>Baseline CRP (mg/l)</td>
<td>2.46 [1.02-5.22]</td>
<td>2.39 [1.18-4.60]</td>
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<tr>
<td>Culprit vessel</td>
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<td>LAD</td>
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<td>44 (57%)</td>
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<tr>
<td>RCA</td>
<td>34 (46%)</td>
<td>33 (43%)</td>
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<tr>
<td>TIMI flow 3 post-pPCI</td>
<td>57 (77%)</td>
<td>53 (69%)</td>
</tr>
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</table>

Continuous variables are summarized as median [interquartile range]. Categorical variables are presented as count (percentage).

Abbreviations: CRP, C-reactive protein; eGFR, estimated glomerular filtration rate (Cockroft-Gault); hsTnT, high-sensitivity troponin T; LAD, left anterior descending; LCx, left circumflex; pPCI, primary percutaneous coronary intervention; RCA, right coronary artery; TIMI, thrombolysis in myocardial infarction.
Figure Legends:

Figure 1. Study flow chart. All patients were screened at the emergency room and consent was sought. Final eligibility was determined in the catheterization department, as per protocol requirements. All exclusions at this stage were due to protocol provisions.

Figure 2. MRI-LGE images. Example of scar delineation using the Segment® software with the weighted area method (infarcted pixels are weighted with their signal intensity). The yellow line denotes the complete affected area (scar), and the pink line a graphical representation of the corresponding weighted area. Microvascular obstruction is indicated in red. For further information, read Heiberg E, et al.12

Figure 3. Myocardial injury biomarkers in the total cohort. Boxplot graphs illustrating the distribution of highest post-MI hsTnT (left) and area under the curve of CK-MB concentration (left) in the total of 151 patients (the thick horizontal black line corresponds to the median, the box to the interquartile range and the whiskers to the range bar extreme values, which are represented by dots and are defined as data points found outside 1.5 times the interquartile range, below or above the 25th and 75th percentiles, respectively).

Figure 4. MRI- and biomarker-defined infarct size in the MRI subgroup. Boxplot graphs illustrating the distribution of infarct size descriptors in the two treatment arms in patients who underwent cardiac MRI (see Figure 3 for explanation of boxplot elements).
Figure 5. A. Correlations between biomarkers and MRI-defined infarct size. Scatterplots of biochemical versus imaging descriptors of infarct size illustrating an expected relationship between these two measures of infarct size. B. Correlations between neutrophil count and MRI-defined infarct size. Scatterplots of maximal post-infarction neutrophil absolute count versus relative (as a proportion of the left ventricular mass) and body-surface-area-indexed absolute infarct size.
Figure 1
Figure 2
Figure 3
Figure 4
Figure 5

A. Spearman's rho 0.77; p<0.001

MRL-LGE relative infarct size (%) vs. Area under the CK-MB curve (ng.h/ml)

B. Spearman's rho 0.67; p<0.001

MRL-LGE relative infarct size (%) vs. Max neutrophil count (µL)

Spearman's rho 0.42; p=0.001

Max hsTnT (pg/ml)

Spearman's rho 0.57; p<0.001

Inferred MRL-LGE absolute infarct volume (mm^3) vs. Max neutrophil count (µL)
Anti-Inflammatory Treatment With Colchicine in Acute Myocardial Infarction: A Pilot Study
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콜치신은 ST분절상승 급성 심근경색증에서 경색의 크기를 줄일 가능성이 있다

초록

배경

염증반응은 ST분절상승 심근경색증(ST-segment-elevation myocardial infarction, STEMI)에서 혈류재개류(ischemia/reperfusion)에 의한 심근손상을 더욱 악화시키는 주요인자이다. 콜치신(cholchicine)은 강력한 항염증제로서, 심혈관질환에서 안전하게 사용할 수 있다. 본 연구는 단기간의 콜치신 사용이 심근경색증에서 경색의 크기를 줄일 수 있는지를 평가하였다.

방법 및 결과

중상 발생 후 12시간 이내의 STEMI 환자 중 일차 관상동맥중재술(primary percutaneous coronary intervention, pPCI)을 시행 받은 환자를 대상으로, 5일간 콜치신 사용군과 위약군으로 무작위 배정하였다. 일차 목표결과는 심근효소 중 크리테인카인세-미ocardial brain fraction(CK-MB)의 총 방출량(area under the curve, AUC)이었다. STEMI 6-9일 후에 일부 환자에서 late gadolinium enhancement를 포함한 심장 magnetic resonance imaging(MRI)을 시행하였다. 연구에는 151명이 포함되었고, 그 중 60명에서 MRI를 시행하였다. CK-MB는 콜치신군에서 3,144(interquartile range (IQR): 1,754-6,940)ng h/mL로 나타나, 위약군의 6,184(IQR: 4,456-6,980)ng h/mL보다 유의하게 작았다(P<0.001). MRI로 확인한 경색의 크기 또한 콜치신군에서 18.3(IQR: 7.6-29.9) mL/1.73m²으로 위약군의 23.2(18.5-33.4)mL/1.73m²에 비해 유의하게 작았다(P=0.019). 뿐만 아니라, 좌심실 심근의 전체 용적이 대비한 경색 크기의 비율도 13.0(IQR: 8.0-25.3)%와 19.8(IQR: 13.7-29.8)%로 나타나 콜치신군이 유의하게 작았다 (P=0.034).

결론

본 연구 결과는 콜치신이 STEMI 환자에서 효과적일 수 있다는 가능성을 제시한다. 그러나 임상 사건에서의 효과를 포함한 확실한 결론을 위해서는 추가적인 연구가 더 필요하다.