Původní sdělení | Original research article

Coronary ostial assessment of myeloperoxidase level correlated to severity of coronary artery disease

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SOUHRN

Kontext: Myeloperoxidáza se účastní proaterogenních biologických aktivit souvisejících s rozvojem kardiovaskulárních onemocnění včetně vzniku, postupu a akutních komplikací procesu aterosklerózy.
Cíl studie: Naším cílem bylo zjistit vztah mezi hodnotami myeloperoxidázy (MPO) v ústí koronárních tepen a závažností ischemické choroby srdeční (ICHS).
Metody: Populace našich pacientů byly rozdělena do dvou skupin, A a B. Do skupiny A bylo zařazeno 43 pacientů s infarktem myokardu bez elevací úseku ST (non-ST elevation myocardial infarction, NSTEMI), u nichž bylo provedeno koronarografické vyšetření. Skupina B zahrnovala 43 pacientů bez ICHS prokázané zátěžovým EKG nebo zátěžovým vyšetřením perfuze s thalliem. Hodnoty MPO se stanovovaly ze vzorků krve odebrané z ústí koronárních tepen v skupině s ICHS a vzorků periferní krve u obou skupin. Závažnost ICHS se hodnotila pomocí skórovacích systémů Gensini a CASS.
Výsledky: Mezi oběma skupinami byl nalezen významný rozdíl v hodnotách MPO (p = 0,002). Při použití obou skórovacích systémů hodnoty MPO v séru korelovaly se závažností ICHS (Gensini; p = 0,002 a CASS; p = 0,05). Ve skupině s ICHS korelovaly hodnoty MPO ve vzorcích periferní krve i ve vzorcích odebraných z ústí koronárních tepen.
Závěry: Hodnoty MPO v séru korelovaly se závažností ischemické choroby srdeční. Hodnoty MPO v periferní krvi odrážely hodnoty MPO naměřené v krvi odebrané z ústí koronárních tepen. Koronární ostium je jednoduché, přístupné a spolehlivé místo pro odběr vzorků krve z koronárních tepen.

Keywords:
Acute coronary syndrome
Coronary blood sampling
Gensisi score
Myeloperoxidase

ABSTRACT

Background: Myeloperoxidase participates in proatherogenic biological activities related to the evolution of cardiovascular disease including initiation, propagation, and acute complications of atherosclerotic process.
Aim of study: We aimed to identify the relationship between myeloperoxidase (MPO) level at the ostium of coronary arteries and severity of coronary artery disease (CAD) .
Methods: Our study population was divided into two groups: group A and B. Group A included 43 patients with non-ST elevation myocardial infarction (NSTEMI) who underwent coronary angiography. Group B included 43 subjects free from CAD as proved by stress ECG or stress thallium study. MPO level was assessed by coronary osteal sampling of CAD group and peripheral venous sampling of both groups. The severity of CAD was studied using the Gensini & CASS scores.
Results: There was a significant difference in MPO level between both groups (p = 0.002) . Serum MPO was correlated to coronary artery disease as evaluated using Gensini score (p = 0.002) & CASS score (p = 0.05). Peripheral venous sample of MPO correlated with coronary osteal samples in CAD group.
Conclusions: Serum MPO was correlated to severity of coronary artery disease. The peripheral venous level of MPO reflected the osteal coronary levels of MPO. Coronary ostium is a simple, accessible and reliable site for coronary sampling.

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Introduction

Myeloperoxidase (MPO) participates in proatherogenic biological activities related to the evolution of cardiovascular disease, including initiation, propagation, and acute complications of atherosclerotic process.[1,2]

Potential mechanisms that may relate to MPO promoting vascular disease include the following: stimulating conversion of low-density lipoprotein (LDL) into an atherogenic form,[3] selectively modifying apolipoprotein A-1, and generating dysfunctional high-density lipoprotein (HDL),[4] promoting endothelial dysfunction, promoting vulnerable plaque,[5] and promoting myocardial dysfunction and abnormal ventricular remodeling after myocardial infarction.[6]

Thereby, MPO and its inflammatory cascade represent an attractive target for prognostical investigation and therapeutics in atherosclerotic cardiovascular disease (Fig. 1).[7]

Several studies point to the independent effect of MPO levels in the evolution of disease and incidence of events in patients with acute coronary syndrome. However, the additional predictive value of MPO levels in the cardiovascular risk assessment and as a marker of plaque vulnerability, is still not consistent.[9]

It is also possible that MPO is released systemically from other sources reflecting a systemic inflammation state. In order to convincingly explore and appropriately interpret this clinically important issue the source of MPO needs to be determined. This could be suitably done by measuring and comparing intracoronary and systemic values of MPO.[10] Selective catheterization of the coronary circulation may be one approach for blood sampling either through the coronary sinus (CS) catheterization or the coronary arterial ostium.[11] The invasive nature of CS cannulation carries an increased risk from the additional venous access site, transient supraventricular arrhythmias, activation of platelet and thrombin production and failure to achieve a stable catheter position with adequate exclusion of atrial blood.[12]

Emerging evidence seems to suggest that plasma levels from coronary artery ostium can be used to estimate blood indices. This may prove quite attractive in quantifying the 'local' environment, as it can be included in the left-heart catheterization procedure without the need for additional right-sided instrumentation.[13]

The current study aimed to evaluate MPO level in CAD patients and compare coronary osteal with peripheral venous samples of MPO.

Subjects and methods

This is a case-control study (which was approved by the local ethical committee of Cairo University), it included 86 subjects recruited over 3-month duration and they were divided into two groups. Group A included 43 patients with non-ST elevation myocardial infarction (NSTEMI) who were admitted to the Cardiovascular department of Cairo University Hospital and underwent coronary angiography. Group B included 43 subjects without CAD proved by stress ECG or stress thallium study. MPO level was assessed by coronary osteal sampling of CAD group and peripheral venous sampling of both groups. The severity of CAD was quantitated using the Gensini & CASS scores.

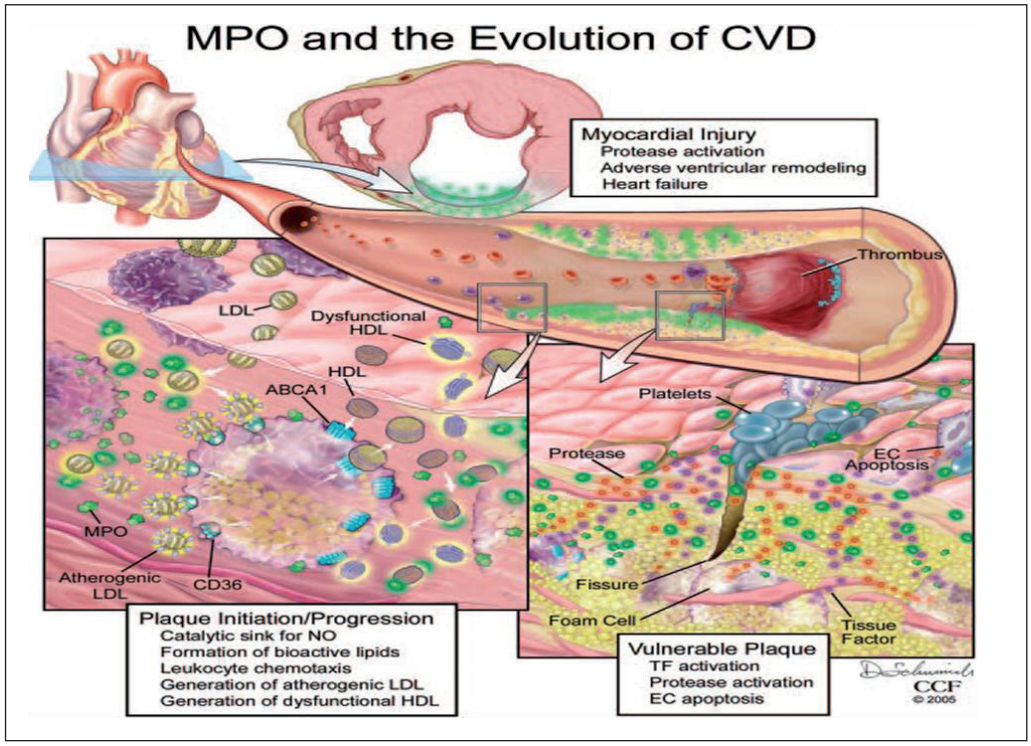

Fig. 1 – Scheme illustrating multiple processes throughout the evolution of atherosclerosis in which MPO is implicated.[8] EC – endothelial cell; MPO – myeloperoxidase; NO – nitric oxide; TF – tissue factor.

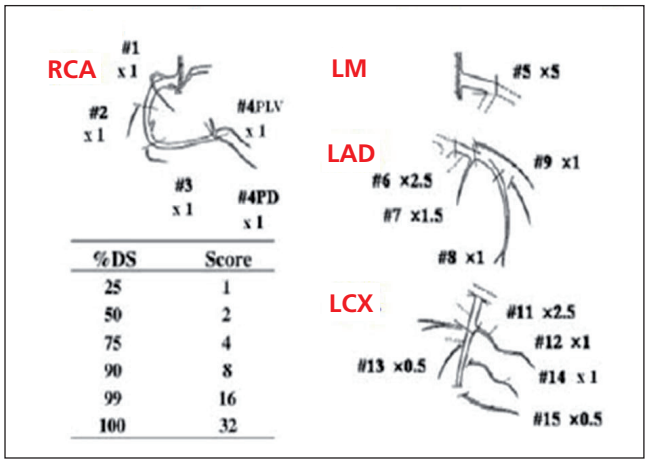

Fig. 2 – Calculation of Gensini score.[16] DS – degree of stenosis; LAD – left anterior descending; LCX – left circumflex; LM – left main; RCA – right coronary artery.

Coronary Artery Surgery Study (CASS) score

This is the number of vessels with significant stenosis (for left main coronary artery 50% or greater and for others 70% or greater reduction in luminal diameter). The score ranged from 0 to 3, depending on the number of vessels involved. Score 0 = no vessel involvement. Score 1 = single vessel involvement. Score 2 = double vessel involvement. Score 3 = triple vessel involvement.[14]

Gensini score

The score was computed by assigning a severity score to each coronary stenosis according to the degree of luminal narrowing and its geographic importance (Fig. 2).

Reduction in the lumen diameter, and the appearance of concentric lesions and eccentric plaques were evaluated (0–25%, 25–50%, 50–75%, 75–90%, 90–99%, and 100%, stenosis is scored as, 1, 2, 4, 8, 16, and 32 points, respectively).

Each principal vascular segment was assigned a multiplier in accordance with the functional significance of the myocardial area supplied by that segment: the left main coronary artery × 5; the proximal segment of left anterior descending coronary artery (LAD) × 2.5; the proximal segment of the circumflex artery × 2.5; the mid-segment of the LAD × 1.5; the right coronary artery, the distal segment of the LAD, the posterolateral artery, and the obtuse marginal artery × 1; and others × 0.5.[15]

Myeloperoxidase assessment

MPO was measured using a Human Myeloperoxidase Quantikine ELISA Kit. Peripheral venous blood samples were collected from each subject of both groups from the peripheral veins. Coronary arterial blood samples were collected from CAD group as well via Judkins catheter after engaging the left main coronary ostium. All catheters and sheaths were flushed with a small solution of 0.5% heparinized normal saline solution (0.9% sodium chloride).

The positions of the catheters were verified under fluoroscopy and following iodinated contrast injection. The first 5 mL of aspirated blood was discarded each time prior to assay sampling.

Statistical analysis

Data were coded and entered using the statistical package SPSS (Statistical Package for the Social Sciences) version 17. Data were summarized using mean and standard deviation, median in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Comparisons between quantitative variables were done using the non-parametric Kruskal–Wallis and Mann–Whitney tests. For comparing categorical data, Chi-square ($\chi 2$) test was performed. Exact test was used instead when the expected frequency is less than 5. Correlations between quantitative variables were done using Spearman correlation coefficient. *P*-values less than 0.05 were considered as statistically significant.

Results

The mean age of studied subjects was 47.5±6.2 years (group A 50.0±6.3 yrs and group B 45.0±5.0 yrs). Baseline characteristics and clinical data of the study groups are summarized in Table 1.

Coronary angiography

Group A included 43 patients who underwent coronary angiography. Eighteen patients (41.8%) had a single vessel disease, 10 patients (23.2%) had a two-vessel disease and 15 patients (34.8%) had a three-vessel disease. Gensini score ranged from 7 to 158 with a mean of 56.8±40.7. Group B included 43 subjects all underwent non-invasive stress test; 30 (69.7%) had exercise treadmill ECG test, and 13 (30.2%) had TC^{99}sestamibi myocardial scan. All tests were negative for CAD.

Myeloperoxidase serum level evaluation

Levels were measured from a coronary artery ostial blood sample (MPO-c) in group A and from a peripheral venous blood sample (MPO-p) in both groups. In group A it ranged from 11–125 with a mean 63.7±37.0 mg/dL. In group B it ranged from 3 to 17 with a mean 9.1±3.8 mg/dL.

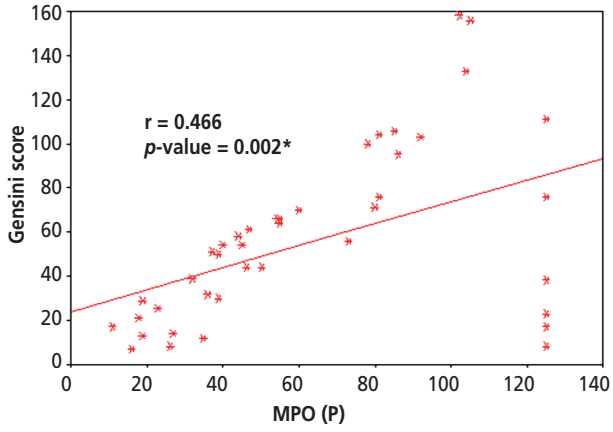

Fig. 3 – Peripheral venous blood sample of myeloperoxidase (MPO) and Gensini score.

Table 1 – Baseline and clinical characteristics of the studied groups

Variable		Group A N = 43	Group B N = 43	Total N = 86	*p*-value
Age	(Mean±SD)	50.02±6.35	45.02±5.01	47.52±6.22	>0.05
	Range	36–62	36–58	36–62	
Sex	Male	25 (58.14%)	24 (55.82%)	49 (56.98%)	>0.05
	Female	18 (41.86%)	19 (44.18%)	37 (43.02%)	
Diabetic (DM)		24 (55.82%)	10 (23.25%)	34 (39.53%)	<0.05
Hypertensive (HTN)		25 (58.14%)	18 (41.86%)	43 (50%)	>0.05
Smoker		17 (39.53%)	18 (41.86%)	35 (40.70%)	>0.05
Dyslipidemic		22 (51.16%)	17 (39.53%)	39 (45.35%)	>0.05
Family history		14 (32.56%)	9 (20.93%)	23 (26.74%)	<0.05

Table 2 – MPO-p: myeloperoxidase levels in peripheral venous circulation

			Paired differences		Paired Samples Test
	Range	Mean±SD	Mean	SD	*p*-value
MPO-p	11–125	63.7±37.0	–2.279	2.557	Non significant
MPO-c	12–125	66.0±37.1			

MPO-c – myeloperoxidase levels in coronary arteries.

No statistical differences were found between the measured MPO-p and the MPO-c in group A (Table 2).

Moreover, peripheral and coronary levels of MPO was positively correlated with Gensini score (p <0.05 and r: 0.45). Using CASS score, the association between level of MPO, and coronary artery disease severity was borderline significant (p = 0.05) (Fig. 3).

Discussion

The current study enrolled 86 patients, group A included 43 angiographically documented CAD patients and group B included 43 subjects proved to be free of CAD. MPO levels were studied in systemic venous circulation in both groups and in coronaries through osteal coronary sampling in group A.

In comparison to multiple trials evaluating the MPO level in patients suffering from stable, acute coronary syndrome[17] and myocardial infarction,[19] our study was applied on NSTEMI patients.

Our results went with the stream of the results of above mentioned and lot of published trials that found an association between CAD and MPO level.[20–22] However this association (in our study) was prominent using Gensini score for evaluation of CAD severity and was borderline when using CASS score that may be related to small number of studied patients.

Düzgünçiet et al.[20] demonsterated the same results .Moreover,he found a positive correlation to coronary calcium scores (r = 0.433, p = 0.017) as well.

Zhang et al.[21] found that both the leukocyte and blood MPO levels were significantly higher in patients with CAD than in controls (p <0.001).

Cavusoglu et al.[22] found that myeloperoxidase was independently predictive of the presence of multivessel disease (≥ 2 vessels) on coronary angiography.

On the other hand our results showed some differences when compared to other studies.[23,24] Lukas Kubet et al.[24] studied 557 patients with stable CAD who underwent elective coronary angiography and found that MPO levels did not differ significantly between patients with or without CAD. The reason for the differences in results can be attributed to different methodological principles of research and different creation of the test sample as well as the different size of the study population.

A large body of literature has broadly evaluated MPO level through a samples withdrawn from systemic circulation. However, in only a few studies the level of MPO was measured in coronary circulation.

In our study we have withdrawn a peripheral venous as well as coronary samples. Serum level of MPO was correlated to the coronary arterial serum levels and the difference was not statistically significant.

This result is compatible with multiple trials[25,26] who sampled blood from occluded coronary artery via an export aspiration catheter. Coronary samples in our study were withdrawn from the ostial coronary region by the diagnostic catheter without use of aspiration catheter or microcatheters. Kirbiš et al.[26] studied 20 patients, 11 of them had acute coronary syndrome and the other 9 patients had stable angina. Intracoronary blood samples were taken at the culprit lesion in the coronary artery in patients with ACS and from any coronary artery in the other two groups via a microcatheter, along with systemic blood samples from the femoral vein and artery. They found no difference between coronary and peripheral samples.

We considered coronary ostial sampling as a more simple approach for coronary sampling than coronary sinus sampling or coronary sampling using aspiration or microcatheters.

Many studies evaluated blood indices (other than MPO) through samples collected from the coronary ostium. Kabbani et al.[13] evaluated soluble markers of platelet activation (e.g. P-selectin and CD40 ligand [CD40L]) in blood samples acquired from the coronary ostium, aortic root, coronary sinus, and the femoral vein.

The study showed that P-selectin levels measured from both the coronary ostium and the coronary sinus showed no difference.

Aggarwal et al.[27] measured the concentrations of C-reactive protein (CRP), interleukin (IL)-6, IL-1 receptor antagonist, and soluble CD40 ligand (sCD40L) in blood drawn from patients before percutaneous coronary intervention from the femoral artery and from a guide catheter after engagement of the culprit coronary artery. The concentrations of CRP and IL-6 were similar in coronary ostial and peripheral blood. Most of the published series examined the MPO level in the systemic circulation of CAD patients. Only few studied the level of MPO in coronary arteries. Moreover most authors collected coronary samples from the coronary sinus, only few collected them directly from the coronary arteries through microcatheter or aspiration catheter. To the best of our knowledge, it is the first trial to assess coronary meloperoxidase level through coronary osteal sampling.

Conclusion

Serum MPO is correlated to severity of coronary artery disease. The peripheral venous serum level of MPO reflects the intracoronary arterial serum levels of MPO. Coronary ostium is a simple accessible, and reliable site for coronary sampling.

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Conflict of interest
None declared.

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