Association of plasma interleukin-6 with infarct size, reperfusion injury and adverse remodeling after ST- elevation myocardial infarction

Tiller C[1], Reindl M[1], Holzknecht M[1], Lechner I[1], Schwaiger J[3], Brenner C[1]

Mayr A[2], Klug G[1], Bauer A[1], Metzler B[1], Reinstadler SJ[1]

[1] University Clinic of Internal Medicine III, Cardiology and Angiology, Medical University of Innsbruck, Austria
[2] Department of Radiology, Medical University of Innsbruck, Austria
[3] Department of Internal Medicine, Academic Teaching Hospital Hall in Tirol, Austria

Background

Little is known about the clinical relevance of interleukin (IL)-6 in patients with acute ST-elevation myocardial infarction (STEMI). This study examined the possible associations of plasma IL-6 concentrations with infarct size (IS), reperfusion injury and adverse left ventricular remodeling (LVR), in STEMI patients treated with primary percutaneous coronary intervention (PCI).

Methods

We prospectively included 170 consecutive STEMI patients (median age 57 years, 14% women) treated with primary PCI between 2017-2019. Blood samples for biomarker analyses including IL-6 were collected at day 2. Left ventricular ejection fraction (LVEF), IS, and reperfusion injury (microvascular obstruction [MVO] and intramyocardial haemorrhage [IMH]) were determined using cardiac magnetic resonance imaging at day 4 (interquartile range [IQR]:3-6). LVR was defined as ≥10% increase in left ventricular end-diastolic volume from baseline to 4 months CMR follow-up.

Conclusions

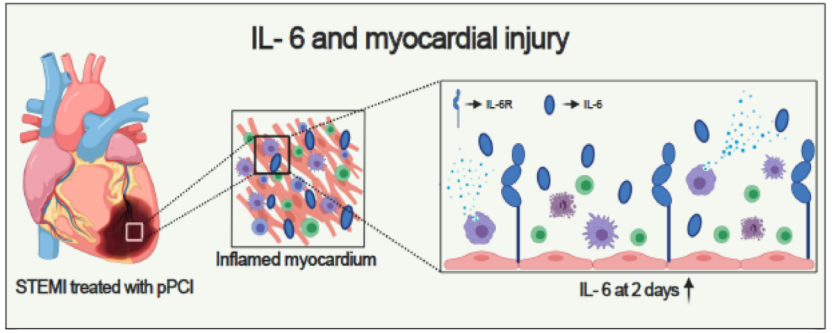
High concentrations of circulating plasma IL-6 at day 2 after primary PCI for STEMI were independently associated with worse myocardial function, larger infarct extent, more severe reperfusion injury and a higher likelihood for LVR, suggesting IL-6 as a useful biomarker of more serious outcome and potential therapeutic target.

Results

	Total population (n=170)	IL-6 < 17 ng/l (n=85, 50%)	IL-6 ≥ 17 ng/l (n=85, 50%)	p-value
Age, years	57 [51-66]	55 [50-65]	59 [55-70]	**0.002**
Female, n (%)	22 (14)	10 (12)	16 (19)	0.201
Body mass index, kg/m²	27 [25-30]	26 [25-30]	27 [25-30]	0.886
Hypertension, n (%)	83 (52)	45 (53)	42 (49)	0.645
Current smoker, n (%)	79 (50)	52 (61)	34 (40)	**0.006**
Hyperlipidemia, n (%)	89 (56)	46 (54)	52 (61)	0.352
Diabetes mellitus, n (%)	19 (12)	5 (6)	15 (18)	**0.017**
Anterior infarct localisation, n (%)	81 (51)	35 (41)	53 (62)	**0.006**
Number of affected vessels, n (%)				0.624
1	100 (59)	53 (62)	47 (55)	
2	47 (28)	22 (26)	25 (30)	
3	23 (13)	10 (12)	13 (15)	
TIMI flow 0 pre-pPCI, n (%)	114 (67)	53 (62)	61 (72)	0.192
TIMI flow 3 post-pPCI, n (%)	149 (88)	81 (95)	68 (80)	**0.002**
Total ischemia time, min	179 [109-282]	166 [107-266]	202 [110-333]	0.339
Door to balloon time, min	24 [11-40]	24 [10-42]	22 [13-38]	0.885
IL-6, ng/l	17 [11-34]	11 [8-13]	33 [24-50]	**<0.001**
Hs-CRP, mg/l	32 [16-52]	19 [11-26]	49 [35-80]	**<0.001**
WBCc, G/l	9 [8-11]	8 [7-10]	10 [8-11]	**0.001**
Hs-cTnT, ng/l	2868 [1556-4942]	1932 [976-3355]	3909 [2633-6307]	**<0.001**

Table 1: Baseline characteristics.

Patients with IL-6 concentrations ≥ median (17ng/l) showed a significantly lower LVEF (43% vs .52%, p<0.001), larger IS (22% vs. 13%, p<0.001), larger MVO (1.9% vs. 0.0%, p<0.001), and more frequent IMH (52% vs. 18%, p<0.001).



LVR was more common in patients with IL-6 ≥ median (24% vs. 9%, p=0.005).

In both linear and binary multivariable regression analysis, IL-6 remained independently associated with lower LVEF (odds ratio [OR]: 0.10, 95% confidence interval [CI] 0.02 to 0.42, p=0.002), larger IS (OR: 5.29, 95% CI 1.52 to 18.40, p=0.009), larger MVO (OR: 5.20, 95% CI 1.30 to 20.85, p=0.020), with presence of IMH (OR: 3.73, 95% CI 1.27 to 10.99, p=0.017) and adverse LVR (OR: 2.72, 95% 1.06 to 6.98, p=0.038). Patients with IL-6 concentrations ≥17ng/l were more likely to experience major adverse cardiac events (p=0.028) during a median follow-up of 12 (IQR: 5-14) months.