Myocardial perfusion in non-infarcted areas in acute coronary syndrome with ST-segment elevation assessed by SPECT perfusion imaging

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INTRODUCTION

Acute coronary syndromes (ACS) are associated with a global slowing of coronary perfusion [1, 2]. The sympathetic activity, increased in patients with myocardial infarction, impairs vasodilator responsiveness in the coronary circulation [2, 3]. A shift towards lactate metabolism in areas of the myocardium not affected by coronary occlusion was observed in animal models [4, 5].

We aimed to examine the myocardial perfusion and viability in non-infarcted areas in patients with first ACS with ST-segment elevation myocardial infarction (STEMI) as assessed by single photon emission computed tomography (SPECT) perfusion imaging, an imaging modality widely accepted for the diagnosis of cardiovascular diseases [6].

METHODS

This is a post hoc analysis of a trial on aspiration thrombectomy in STEMI patients performed between January 2005 and September 2008 [7].

The eligibility criteria were: (1) first STEMI within 12 hours from symptoms onset; (2) culprit lesion in the left anterior descending (LAD) or right coronary arteries (RCA); and (3) culprit Thrombolysis in Myocardial Infarction (TIMI) blood flow grade ≤2 [7]. The exclusion criteria included: (1) cardiogenic shock; (2) culprit in the left circumflex artery (LCX); (3) previous myocardial infarction; and (4) any chronic total coronary occlusion.

Following the angiography, the patients were randomized (1:1) to a group with aspiration thrombectomy or a group with standard primary percutaneous intervention (pPCI) of infarct-related artery (IRA). Immediately after and before the intervention all patients received an intravenous injection of ^{99m}Tc-sestamibi. An index SPECT examination (SPECT I) was performed within 3–5 hours after injection. Follow-up ^{99m}Tc-sestamibi imaging (SPECT II) was performed within 5–8 days after the intervention. Perfusion of the myocardium was assessed in 17 myocardial segments. LAD typically supplies 7 segments while RCA and LCX each supply 5 segments. We used a standard grading scale for visual assessment of perfusion where 0 indicates no perfusion impairment, 1 — mild, 2 and 3 moderate perfusion abnormalities, and 4 — lack of perfusion. The sum of perfusion segmental defect grades for each vessel territory and for the whole myocardium produced respective Summary Defect Score (SDS) indices. Separate SDS for LAD (SDS_{LAD}), RCA (SDS_{RCA}), and LCX (SDS_{LCX}) territories were calculated for SPECT I and SPECT II. Combined SDS for non-infarct-related territory was then calculated. Since in patients with culprit LAD there are 10 remote segments and in patients with culprit RCA there are 12 segments, we normalized the values, and hence normalized SDS for non-infarct-related territory ($SDS_{non\text{-}IRA}$) was either a product of (SDS_{RCA} + SDS_{LCX}) × 1.2 for the culprit LAD or SDS_{LAD} + SDS_{LCX} for the culprit RCA. To avoid bias related to the overlapping of blood supply in apical segments, we also calculated SDS for the basal LAD, basal RCA, basal LCX, and basal non-IRA segments (SDS_{LADBAS}, SDS_{RCABAS}, SDS_{LCXBAS}, and $SDS_{non\text{-}IRABAS}$ respectively). There are two basal segments for every coronary artery, and hence no normalization factor was needed. SPECT examinations were used for the assessment of left ventricular ejection fraction (LVEF).

The study was approved by the local Ethics Committee and was performed in accordance with the Helsinki Declaration. All patients participating in the trial signed informed consent.

Statistical analysis

Continuous data with normal distribution are presented as means with standard deviation while the non-normally distributed are presented as medians with interquartile ranges. Normality was assessed using the Shapiro-Wilk test. Correlations of continuous variables were assessed with the Spearman coefficient. A two-tailed paired sample t-test or Wilcoxon test were used to assess differences between continuous variables. All *P*-values below 0.05 were considered significant. Software MedCalc version 9.3.8.0 (MedCalc, Marierkerke, Belgium) was used for statistical analysis.

Results and discussion

There were 137 (5%) patients enrolled from 3030 patients with STEMI treated between January 2005 and September 2008 [7]. Paired SPECT I and SPECT II examinations with a full dataset enabling SDS evaluation were available for 124 (91%) patients (5 [4%] patients died before the second SPECT, 3 [2%] patients could not be transferred to the nuclear lab due to hemodynamic instability, and in 5 [4%] cases, SPECT data on SDS evaluation for separate segments were not available). There were 88 (71%) male patients with mean (SD) age of 62.9 (11.5) years. LAD was the culprit vessel in 41 (33%) and RCA in 83[67%] patients. Main comorbidities were hypercholesterolemia (n = 93, 75%), hypertension (n = 71, 57%), active smoking (n = 52, 42%), and diabetes mellitus (n = 19, 15%). Before the angiography, all patients received loading doses of acetylsalicylic acid (ASA) (300 mg) and clopidogrel (300–600 mg) (in 110 patients [89%] ASA, and in 91 patients (73%) clopidogrel was initiated before admission). Secondary lesions in non-culprit arteries were identified in 15 (12%) patients. The study results are summarized in Table 1.

Overall, median $SDS_{non\text{-}IRA}$ and $SDS_{non\text{-}IRABAS}$ improved between SPECT I and SPECT II examinations: median (interquartile range [IQR]), 9 (5–14) vs. 7 (4–11); $P < 0.001$ and 4 (2–8) vs. 4 (1–7); $P < 0.001$, respectively.

In subgroup analyses, we observed improvement in $SDS_{non\text{-}IRA}$ and $SDS_{non\text{-}IRABAS}$ between SPECT I and SPECT II both for patients with culprit RCA and patients with culprit LAD.

The median difference in normalized $SDS_{non\text{-}IRA}$ and $SDS_{non\text{-}IRABAS}$ between SPECT I and SPECT II (delta) was larger for culprit LAD than for culprit RCA: –2.4 (–6.3–[–1.2]) vs. –1 (–3–1); $P = 0.005$ and –1 (–3–0) vs. 0 (–1–0); $P = 0.001$ respectively. At SPECT I examination $SDS_{non\text{-}IRA}$

Table 1. Perfusion data at SPECT I and SPECT II examinations. Results are presented as median (interquartile range, IQR) or mean (standard deviation, SD)

Culprit	Perfusion data	SPECT I	SPECT II	*P*-value
Both (124)	$SDS_{non\text{-}IRA}$ median (IQR)	9 (5–14)	7 (4–11)	<0.001
	Normalized $SDS_{non\text{-}IRA}$ median (IQR)	9.8 (5–15.6)	8 (4–12)	<0.001
	$SDS_{non\text{-}IRABAS}$ median (IQR)	4 (2–8)	4 (1.5–7)	<0.001
	SDS_{LAD} median (IQR)	4 (1–20)	4 (2–13)	0.01
	SDS_{LCX} median (IQR)	4 (0–6)	2 (0–4)	<0.001
	SDS_{RCA} median (IQR)	12 (9–15)	8 (6–12)	<0.001
	SDS_{LADBAS} median (IQR)	1 (0–4)	1 (0–3)	0.04
	SDS_{LCXBAS} median (IQR)	2 (0–4)	1 (0–3)	<0.001
	SDS_{RCABAS} median (IQR)	8 (4–9)	6 (3–7.5)	<0.001
	SDS total median (IQR)	24 (16–34)	18 (12–26)	<0.001
LAD (n = 41. 33%)	$SDS_{non\text{-}IRA}$ mean (SD)	12.8 (4.6)	10.3 (5.0)	<0.001
	Normalized $SDS_{non\text{-}IRA}$ mean (SD)	15.4 (5.5)	12.3 (6.0)	<0.001
	$SDS_{non\text{-}IRABAS}$ median (IQR)	8 (4–11)	7 (3–9)	<0.001
	SDS total median (IQR)	36 (31–39)	28 (21–34)	<0.001
RCA (n = 83. 67%)	$SDS_{non\text{-}IRA}$ median (IQR)	7 (4–12)	6 (4–9)	0.01
	Normalized $SDS_{non\text{-}IRA}$ median (IQR)	7 (4–12)	6 (4–9)	0.02
	$SDS_{non\text{-}IRABAS}$ median (IQR)	3 (0–6)	3 (1–5)	0.02
	SDS total median (IQR)	21 (14–26.5)	15 (11–20)	<0.001
	Culprit	LAD	RCA	—
	SPECT I $SDS_{non\text{-}IRA}$ median (IQR)	13 (9.5–16)	7 (4–12)	<0.001
	SPECT I $SDS_{non\text{-}IRABAS}$ median (IQR)	8 (4–11)	3 (0–6)	<0.001
LAD (n = 41. 33%) vs. RCA (n = 83. 67%)	SPECT I normalized $SDS_{non\text{-}IRA}$ median (IQR)	15.6 (11.7–19.2)	7 (4–12)	<0.001
	SPECT II $SDS_{non\text{-}IRA}$ median (IQR)	10 (6.5–14)	6 (4–9)	<0.001
	SPECT II $SDS_{non\text{-}IRABAS}$ median (IQR)	7 (3–9)	3 (1–5)	0.001
	SPECT II normalized $SDS_{non\text{-}IRA}$ median (IQR)	12 (8.1–16.8)	6 (4–9)	<0.001
	Delta (S II – S I) normalized $SDS_{non\text{-}IRA}$ median (IQR)	–2.4 (–6.3–[–1.2])	–1 (–3–1)	0.005
	Delta (S II – S I) $SDS_{non\text{-}IRABAS}$ median (IQR)	–1 (–3–0)	0 (–1–0)	0.001

Abbreviations: BAS, basal; Delta (S II – S I), difference between SPECT II and SPECT I; IQR, interquartile range; IRA, infarct-related artery; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery; SD, standard deviation; SDS, Summary Defect Score; SPECT, single photon emission computed tomography

and $SDS_{non\text{-}IRABAS}$ medians were larger in patients with culprit LAD than with culprit RCA: 13 (9.5–16) vs. 7 (4–12) and 8 (4–11) vs. 3 (0–6); respectively P <0.001 for both comparisons. Also, SPECT II results showed larger $SDS_{non\text{-}IRA}$ and $SDS_{non\text{-}IRABAS}$ medians in patients with culprit LAD: 10 (6.5–14) vs. 6 (4–9); P <0.001 and 7 (3–9) vs. 3 (1–5); P = 0.001 respectively.

There was no difference in median SDS_{nonIRA} and median $SDS_{nonIRABAS}$ between patients with and without secondary stenosis in SPECT I: 8 (4–12.5) vs. 9 (5–14); P = 0.45; 6 (2.5–8) vs. 4 (2–8); P = 0.66, respectively, nor in SPECT II: 6 (2.5–12) vs. 7 (5–11); P = 0.59; 5 (1.5–7) vs. 4 (2–6); P = 0.64, respectively.

The median LVEF was 46% (37%–53%) at SPECT I examination and 45.5% (40%–53%) at the follow-up (P = 0.06). Overall, $SDS_{non\text{-}IRA}$ was inversely correlated with LVEF both at SPECT I and SPECT II examination (R = –0.398; P <0.001 and R = –0.41; P <0.001, respectively). Similar results were obtained for $SDS_{non\text{-}IRABAS}$ (R = –0.437; P <0.001 and R = –0.392; P <0.001, respectively).

Our study is the first to document the presence of global myocardial ischemia detected with SPECT imaging in STEMI patients. The main findings of the study are 1) perfusion in non-infarct-related territories is impaired in the acute phase of STEMI and improves within a week following pPCI; 2) STEMI with culprit lesion located in LAD has a larger impact on perfusion in non-infarct-related territories than inferior STEMI with culprit RCA.

Our data support reports demonstrating that non-culprit artery flow is impaired in patients with STEMI and suggest that slower blood flow impacts perfusion and causes global myocardial ischemia [1]. Gibson et al. [1] showed that thrombolysis improved coronary flow also in non-IRA. Our data extend these findings in relation to tissue perfusion to the patients treated with pPCI. The current report is in line with the data published by Uren et al. [3] who found with the use of positron emission tomography that vessel vasodilator response in patients with myocardial infarction is abnormal even in segments not supplied by the IRA. Moreover, this abnormality may be responsible for the extension of myocardial necrosis. Our findings are in concordance with the results of pathophysiological studies performed on dogs showing that LAD occlusion causes focal necrosis in the remote segments supplied by a patent artery [5].

The finding that STEMI with LAD occlusion is accompanied by especially pronounced perfusion impairment of non-infarct-related territories is similar to the results published by Gibson et al. who showed that STEMI with culprit LAD is associated with slower corrected TIMI frame count [1]. Our results and those presented by Gibson et al. demonstrate the impact of perfusion abnormalities in non-infarcted areas on left ventricular systolic function. Interestingly, we did not find a relation between secondary stenosis in non-IRA and perfusion impairment.

It should be added that currently, the routine use of an aspiration thrombectomy is not standard practice in STEMI patients, however, it does not influence the study findings.

Article information

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