Comparison of coronary artery flow impairment in diabetic and ipertensive patients with stable microvascular angina

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Abstract. – OBJECTIVE: Stable microvascular angina (SMVA) describes patients with angina, findings compatible with myocardial ischemia and normal coronary angiograms. The aim of this study was to evaluate the impact of diabetes on the coronary microcirculation troughs angiography indexes (TIMI Frame Count, Myocardial Blush Grade, Total Myocardial Blush Score) and a new index: Total TIMI Frame Count (TTFC).

PATIENTS AND METHODS: The study population included 310 patients with SMVA that we split into two populations: diabetic-non hypertensive (164 patients) and non-diabetic-hypertensive (146 patients). We calculated, on angiographic images of each patient, TIMI Frame Count (TFC), Myocardial Blush Grade (MBG) and Total Myocardial Blush Score (TMBS) using the protocol described by Gibson and Yusuf. On the basis of Yusuf's experience we imagined a new index: TTFC like sum of the three coronary TFC.

RESULTS: We found a worse coronary microcirculation in diabetic-non hypertensive patients with lower values of TFC, MBG and TMBS ($p = 0.02$), compared with non-diabetic hypertensive. New index TTFC is usually higher in diabetic-non hypertensive than non-diabetic hypertensive patients. Patients with positive scintigraphy had a worse TMBS than patients with a negative one, with a high statistical significance ($p = 0.003$).

CONCLUSIONS: Analysis of diabetic non hypertensive and non-diabetic and hypertensive patients with cardiac syndrome X has led to asses that the diabetic population has a greater involvement of microcirculation. Also the new index, TTFC, proved to be a good marker, in agreement with results of other indexes.

Key Words:
  Microvascular angina, Diabetes mellitus, Microcirculation, Coronary angiography.

Introduction

The term "Stable Microvascular Angina" (SMVA) or Cardiac Syndrome X describe patients with angina, findings compatible with myocardial ischemia, normal coronary arteries on angiography, absence of any other specific cardiac disease (e.g., variant angina, cardiomyopathy, valvular disease)[1-2]. The aim of this study was to compare the impairment of microcirculation in diabetic-non hypertensive and non-diabetic-hypertensive patients. We studied coronary microcirculation troughs angiography indexes like Gibson's index (TIMI Frame Count an Myocardial Blush Grade), Yusuf's index (Total Myocardial Blush Score) and a new index that we imagined, on the basis of Yusuf's experience: the Total TIMI Frame Count (TTFC); we want to see if the results of TTFC are comparable with other indices mentioned.

Patients and Methods

Our study comprehends 310 patients who had been coming to the emergency room for anginal chest pain from January 2004 to May 2011. They were hospitalized to our Division of Cardiology of "Paolo Giaccone" Hospital in Palermo. In this retrospective study, inclusion criteria are their presences of chest pain, at the same time their positive stress test, and coronary arteries free from stenosis at coronary angiography. All patients were subjected to myocardial scintigraphy. Significantly, we excluded patients who had positive biomarkers for myocardial infarction when they arrived to the Emergency Room or during hospitalization. Neither did we consider the mild increase after patients underwent coronary angiography, nor those who had ischemic heart disease in history. Our sample was divided in two groups: diabetic-non hypertensive patients (164 patients) and non diabetic-hypertensive patients (146 patients). On the basis of the angiographic images, TIMI Frame Count and Myocardial

Blush Grade were calculated for each patient. The TIMI Frame Count was calculated according to three main coronary arteries (LAD = left anterior descendent artery; CX = circumflex coronary artery; RCA = right coronary artery). It was used the protocol described by Gibson et al[3]. We did this to make them comparable with those reported in literature[3,4]. Under the same calculation principle, the Myocardial Blush Grade was also calculated carefully following the protocol described by Gibson et al[3]. Besides, we used a new index proposed by Yusuf et al[5], the Total Myocardial Blush Score (TMBS). It was obtained summing up the Myocardial Blush Grade of each coronary area. On the basis of the experience by Yusuf et al, we intended to evaluate another index the Total TIMI Frame Count (TTFC), which was obtained from the sum of the TFCs of the three coronary arteries. We were also trying to evaluate whether the results obtained through TTFC were comparable with the other indices we mentioned, and the aim was to use this new index for a more comprehensive view of the coronary microcirculation.

Statistical Analysis

We used a two-tailed *t*-Student test to determine the statistical significance of differences between continuous variables. A *p*-value < 0.05 was considered significant.

Results

Our sample compared two groups: diabetic-non hypertensive (164 patients) and non diabetic-hypertensive patients (146 patients). We studied this disease to determine whether these patients had a greater involvement of microcirculation, compared with hypertensive-non diabetic patients. We combed the rate of perfusion through the Gibson coronary indexes and we saw that patients with diabetes mellitus and chest pain had a longest TFC of three major coronary arteries, than non-diabetics that indicates slow flow in diabetes coronary microcirculation (Table I).

Then we studied coronary microcirculation perfusion through Yusuf index: we found lower MBG on three coronary arteries and TMBS (*p* = 0.02) in diabetic-no hypertensive than non-diabetics hypertensive patients, with good statistical significance (Figure 1). Finally, the index suggested by us, the TTFC, showed a value greater in diabetics than non-diabetics, although not reaching

Table I. Comparison of TFC, MBG and TMBS between diabetic – non hypertensive and hypertensive –non diabetic patients.

	Diabetic- non ipertensive (164 patients)	Ipertensive-non diabetic (136 patients)	*p*-value
MBG LAD	2.2 (± 0.4)	2.4 (± 0.5)	0.03
MBG RCA	2.2 (± 0.4)	2.3 (± 0.47)	NS
MBG CX	2.1 (± 0.36)	2.3 (± 0.4)	0.04
TMBS	6.6 (± 1.06)	7 (± 1.16)	0.02
cTFC LAD	45.7 (± 12.5)	41 (± 11,6)	NS
TFC RCA	25.6 (± 6.5)	25.1 (± 6.3)	NS
TFC CX	24 (± 5.4)	21 (± 4.7)	0.05

LAD = left anterior descendent artery; CX = circumflex coronary artery; RCA = right coronary artery.

statistical significance, probably because our population has increased in future studies (Figure 2). We think that this new index may provide further information on the overall rate of perfusion of microcirculation and it can help the doctor to take up, with better security, adequate therapy to combat the impairment of microcirculation.

Discussion

The use of coronary angiography and indexes like TFC and Total TFC, introduced by us, may be a useful tool to evaluate coronary microvascular alterations. MBG (so also the Total Myocardial Blush Score introduced by Yusuf) has proved a reliable marker of microvascular dysfunction well correlated with TFC and scintigraphy results. These studies, therefore, can be used as a source to be predictive for future coronary artery
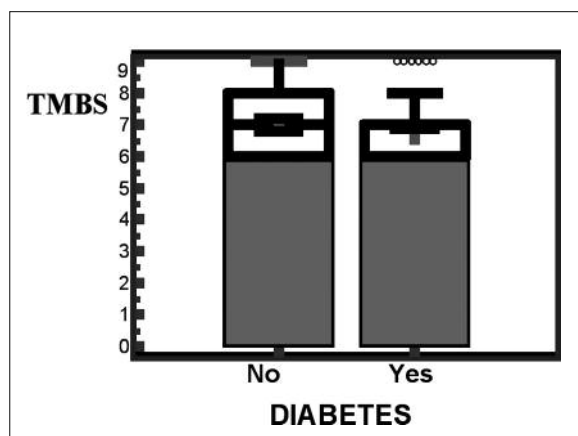

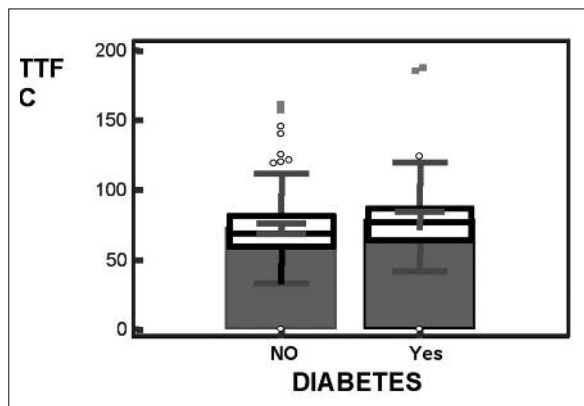**Figure 1.** TMBS in diabetic patients and non diabetic.

Figure 2. New index TTFC in diabetic patients and non patients.

disease. Therefore, these patients should be followed with a careful follow-up to assess any worsening of coronary artery stenosis, with greater attention to those who have cardiovascular risk factors, especially hypertension, which is often present in patients and that is, along with diabetes, a major cardiovascular risk factor, therefore the need to maintain blood pressure levels lower than in non-diabetics is a priority, as the guidelines say[6]. There are few prospective studies on the prognosis of these patients, a long-term follow-up of these subjects should deserve more attention. As far as therapeutic strategies, many studies have shown that after prolonged treatment, as in hypertensive diabetic patients, the coronary reserve may increase[7]. Studies show that the clinical improvement of these patients is to be attributed to the role played by therapy on processes that are responsible for myocardial perfusion defects as alterations in repair mechanisms of microcirculation which was found to be damaged at both structural and physiological[8,9]. The disease state of microcirculation in diabetic patients with SMVA allows us to affirm the absolute necessity to focus on this population (it is necessary to start early an appropriate treatment and it is necessary to follow a long-term follow-up) because this population have a subclinical microcirculation disease without clinical evidence, which could lead to an alteration of the quality of their lives in the future[10].

Conclusions

Analysis of diabetic non hypertensive and non-diabetic and hypertensive patients with cardiac syndrome X has led to asses that the diabet-ic population has a greater involvement of microcirculation. The use of coronary angiography indexes like TFC, MBG, TMBS may be a useful tool to evaluate coronary microvascular alterations in diabetic patients. Also the new index, TTFC, proved to be a good marker, in agreement with results of other indexes.

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Conflict of Interest

The Authors declare that there are no conflicts of interest.

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