

SUPPLEMENTARY DATA

Supplementary data 1: Angiography procedure and coronary collaterals grading

Severity of coronary artery disease(single, 2 or 3-vessel-disease) was defined as the presence of at least one significant($\geq 50\%$) stenosis in each of the 3 major coronary vessels. Anterograde blood flow was graded with the use of the TIMI classification. A complete coronary occlusion was defined as a 100% stenosis associated with a TIMI grade flow=0 or 1. In patients with more than one occluded coronary artery, one was randomly selected for further analysis of collateral vessels.

The flow in the collateral vessels was graded with the use of 2 previously validated semi-quantitative methods; the “Collateral flow grade” and the “Recipient filling grade”(also known as the modified Rentrop Classification) were chosen because they have been previously validated and are considered complementary¹². The “Collateral flow grade” mainly appreciates the size of the collateral itself whereas the “Recipient filling grade” is more focused on the resulting flow in the occluded vessel¹².

1) *Collateral flow grade* : 0=no flow in the collateral; 1=the collateral is barely apparent; dye is not visible throughout the cardiac cycle but is present in at least 3 consecutive frames; 2=the collateral is moderately opaque but is present throughout at 75% of the cardiac cycle; 3=the collateral is well opacified and the column of dye is well defined but is < 0.7 mm wide throughout the majority of its length; 4=the collateral is well opacified, fills antegrade, and is very large, > 0.7 mm in diameter throughout its entire length. In patients with more than one collateral vessel, the collateral vessel with the highest “collateral flow grade” value was used for further analysis.

2) *Recipient filling grade(Modified Rentrop Classification)* : 0=no angiographically apparent collaterals; 1=apparent collaterals extend into a region of myocardium with no angiographically apparent recipient vessel; 2=minimal recipient filling by collaterals is manifested by minor side branch filling and no epicardial artery or epicardial side branch filling; 3=Moderate recipient filling by collaterals is manifested by

complete filling of epicardial side branches and partial filling of a major epicardial artery; 4=there is complete filling of a major epicardial segment. In patients with more than one collateral vessel, the highest “recipient filling grade” value was used for further analysis.

Supplementary data 2: Isolation, culture and phenotyping of Colony forming unit endothelial cells

Peripheral blood mononuclear cells were isolated by ficoll density gradient centrifugation(Eurobio) from 20 mL blood sample and plated on fibronectin-coated six-well plates in EndoCult[®] Medium. After 48 hours, non-adherent cells were collected and plated in replicate fibronectin-coated 24-well plates. Colonies were quantified three days later. Endothelial phenotype was confirmed by immunofluorescent staining for endothelial specific markers(Von Willebrand factor and KDR), and typical uptake of 1,1'-dioctadecyl-3,3,3',3'-tetramethylindocarbocyanine perchlorate-acetylated low density lipoprotein(Dil-acLDL Biomedical Technology)¹⁶. Colony forming units endothelial cells(CFU-ECs) were counted as previously described¹⁵. Results were expressed as number of colonies/ mL. Measurement of VEGF concentration of supernatant was performed as previously described¹⁷.

Supplementary data 3: Summary of previous studies investigating the impact of diabetes mellitus or metabolic syndrome on coronary collateral development in patients with chronic coronary artery disease

| Author | Patients' selection | Total population (n) | Patients with coronary occlusion(n) | Data on duration of occlusion | Method of analysis of collaterals | Effect of Diabetes or Metabolic syndrome |
|-------------------------|----------------------------|-----------------------------|--|--------------------------------------|--|---|
| Ilia ²³ | Angiography | 231 | 103 | No | Angiography | D : No effect |
| Abaci ²⁵ | Angiography | 410 | Unknown | No | Angiography | D : Decrease collaterals |
| Mélidonis ²⁸ | Angiography | 690 | 183 | No | Angiography | D : Increase collaterals |
| Kilian ²⁶ | Angiography | 200 | 200 | No | Angiography | D : Decrease collaterals |
| Kornowski ²⁴ | Angiography | 112 | 112 | No | Angiography | D: No effect |
| Werner ²⁷ | PTCA | 90 | 90 | Yes | Doppler wire | D: Decrease collaterals in some subgroups |
| Olijohek ⁷ | PTCA | 227 | 24 | No | Angiography | MS: No effect |
| Present study | Angiography | 387 | 387 | Yes | Angiography | MS : Decrease collaterals |

D=Diabetes mellitus; MS=Metabolic syndrome