Supplementary material

Wierzbowska-Drabik K, Picano E, Cortigiani L, Kasprzak JD; on behalf of Stress Echo 2020 study group of the Italian Society of Echocardiography and Cardiovascular Imaging (SIECVI). Comparison of coronary flow reserve feasibility in different stress echocardiography protocols: dobutamine, dipyridamole, exercise and rapid pacing. Pol Arch Intern Med. 2021; 131: 830-839. doi:10.20452/pamw.16035

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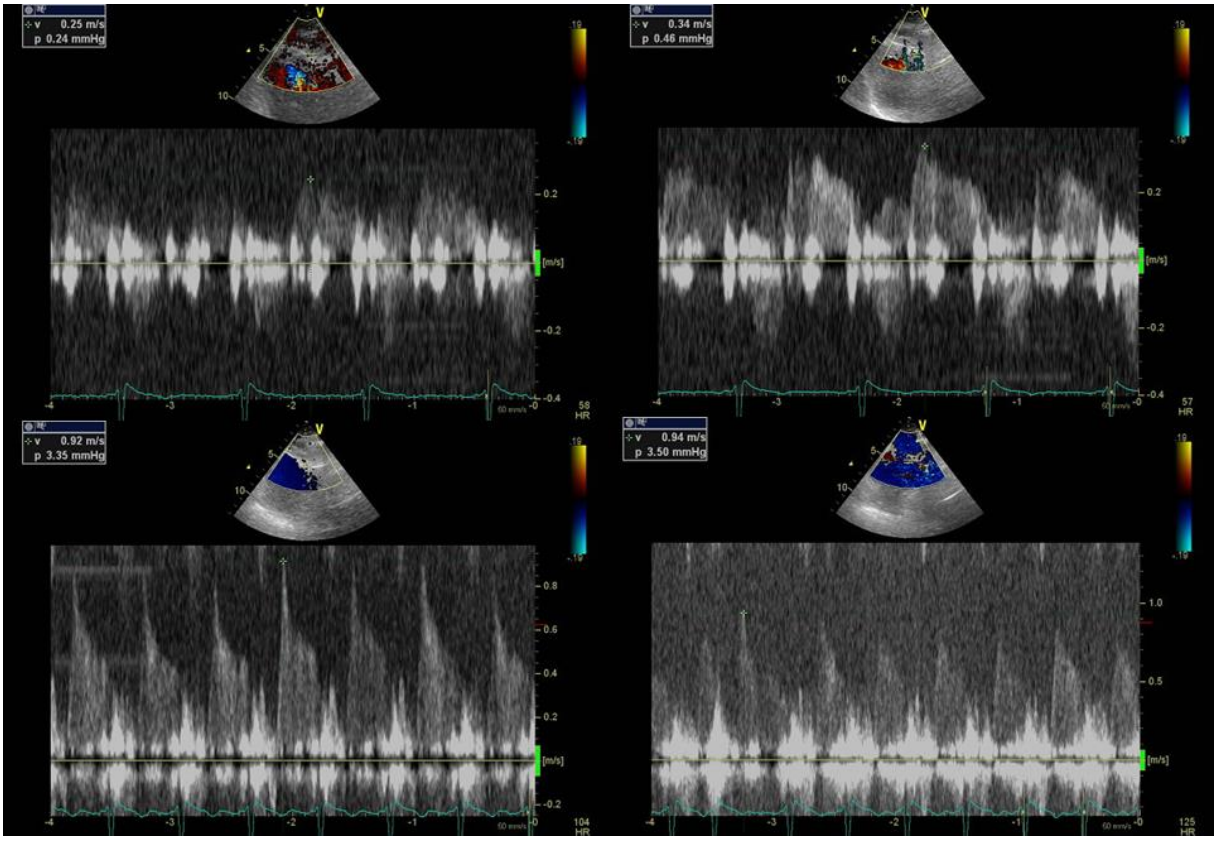
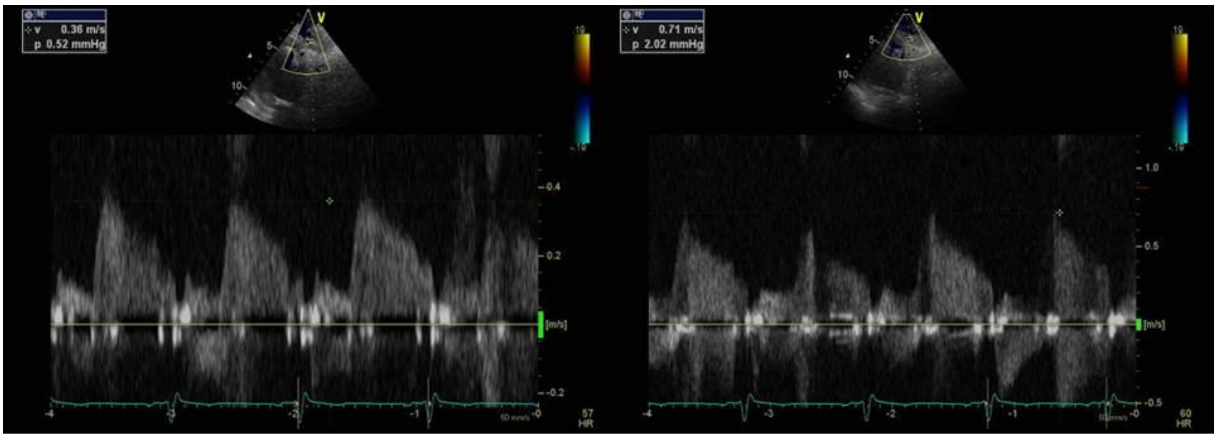
Figure S1.



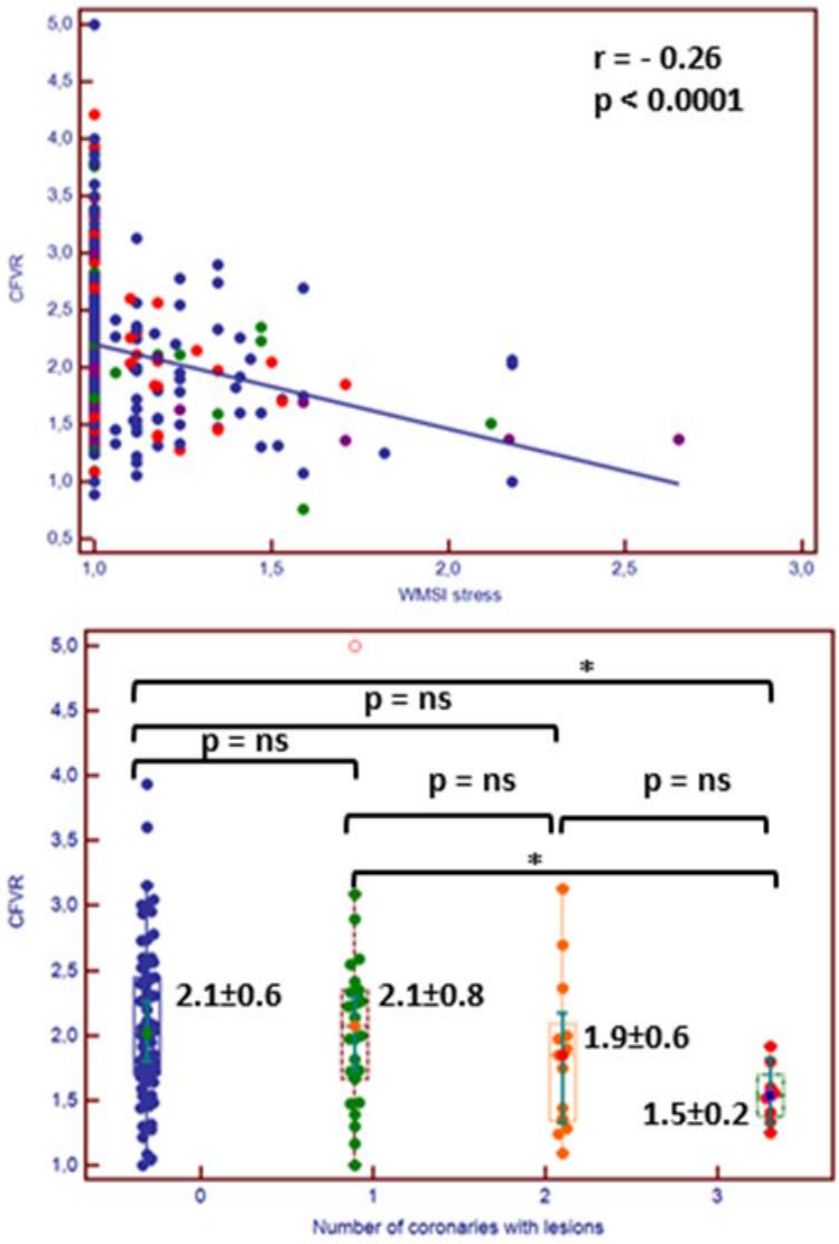
Panel A. Negative, asymptomatic dobutamine study of an 82 year-old-woman with a normal high value of coronary flow velocity reserve, CFVR = 3.7, illustrating good feasibility of left anterior descending artery, LAD, flow recording at all stages of dobutamine as well as significant independence of LAD flow from heart rate, HR, during the study.

The upper left panel shows LAD at rest - 25 cm/s. The upper right panel displays an increase in flow velocity to 34 cm/s at a low dose of 10 μcr/kg/min (despite the similar HR of 58 and 57 bpm, respectively). The lower left panel presents the achievement of the maximal repeatedly measured LAD flow velocity of 92 cm/s at 104 bpm at a medium dobutamine dose of 20 μcr/kg/min. The lower right panel shows a maximal registered velocity of 94 cm/s at the peak of the study which was finished at a dose of 30 μcr/kg/min. A 94 cm/s velocity was registered after an extrasystolic beat, hence a 92cm/s value was taken for CFVR calculation. HR at rest - 58 bpm, at peak - 125 bpm. Follow-up without cardiac events. Angiography not performed.



Panel B. Dipyridamole study positive with wall motion score index, WMSI, increased from 1.18 to 1.35 with slightly lowered values of coronary flow velocity reserve, CFVR = 1.97 in 82-year-old-female patient with history of surgical revascularisation, including left internal mammary artery, LIMA, to LAD implantation. HR at rest 57, at peak 60 bpm, good result of by-pass implantation in coronary angiography, but 80% stenosis in native 1st marginal branch, submitted to successful percutaneous coronary intervention.

Figure S2.



Upper panel. Correlation of coronary flow velocity reserve (CFVR) with wall motion score index (WMSI).

Blue points - dobutamine (DOB), red – dipyridamole (DIP), green - exercise (EXE), violet - pacing (PAC).

Lower panel. Correlation of coronary flow velocity reserve (CFVR) with the number of stenosed arteries in patients with performed coronary angiography showing significant decrease of values in patients with three-vessel coronary artery disease.

Table S1. Comparison between positive and negative stress echocardiography as assessed visually.

Variable	**Group 1, Positive SE n = 27**	**Group 2, Negative SE, n= 342**	***P* value**
Age, years	70 (65-78)	68 (61-74)	0.13
Body mass, kg	70 (63.5-79.8)	76 (67-87)	0.06
BSA, m^2	1.79 (1.66 - 1.89)	1.85 (1.72 - 2.02)	0.06
BMI, kg/m^2	26.5 (23.7 – 30.2)	27.7 (24.9 – 30.9)	0.2
HR rest, bpm	62 (56- 75)	65 (59 - 73)	0.95
DBP rest, mmHg	79 (70- 85)	78 (69- 84)	0.83
SBP rest, mmHg	144 (125- 153)	138 (124 - 152)	0.81
EF rest, %	59 (47- 65)	64 (57- 68)	=0.01
WMSI rest	1.06 (1.0 – 1.323)	1.0 (1.0 – 1.0)	<0.001
B lines rest, number *	0 (0-0); (0-2)	0 (0-0); (0-11)	0.5
LAD rest velocity, cm/s	30 (22- 36)	25 (22- 31)	0.09
HR peak, bpm	125 (100- 132)	128 (106- 135)	0.45
DBP peak, mmHg	75 (67- 85)	75 (67- 85)	0.83
SBP peak, mmHg	135 (116 – 159)	138 (122 – 159)	0.64
EF at peak, %	60 (44 – 68)	68 (62 – 73)	<0.001
WMSI at peak	1.24 (1.12 – 1.47)	1.0 (1.0 – 1.0)	<0.001
B lines peak, number*	0 (0-0); (0-14)	0 (0-0); (0-6)	0.91
LVCR	1.23 (1.06 – 1.6)	1.50 (1.16 – 1.98)	0.02
LAD peak velocity, cm/s	49 (34 – 65)	54 (45 – 65)	0.07
CFVR	1.71 (1.47 – 2.03)	2.06 (1.74 – 2.47)	<0.001
HRR	1.79 (0.36)	1.84 (0.46)	0.58
ΔWMSI	0.12 (0.11 – 0.18)	0 (0 – 0)	<0.001
Coronary angiography, number, %	18 (66.6%)	111 (32.5%)	<0.001
Follow-up – combined events, number, %	11 (40.7%)	25 (7.3%)	<0.001

CFVR- coronary flow velocity reserve, DPB- diastolic blood pressure, EF- ejection fraction, HR- heart rate, HRR- heart rate reserve (HR peak/HR rest ratio), LAD- left anterior descending coronary artery, LVCR- left ventricular contractile reserve (Force at peak/Force rest ratio; Force = SBP/LVESV, LVESV left ventricular end-systolic volume), SBP- systolic blood pressure, SE- stress echocardiography, WMSI- wall motion score index, ΔWMSI- delta of wall motion score index (difference between peak and rest WMSI).

Table S2. Comparison between patients with impaired (<2) and normal (≥2) coronary flow velocity reserve.

Variable	**Group 1, Impaired CFVR n = 146**	**Group 2, Normal CFVR, n= 195**	***P* value**
Age, years	70 (63 – 71)	67 (61 – 72)	0.006
BMI, kg/m^2	27.2 (25 – 30.1)	28.3 (25 – 31.6)	0.25
HR rest, bpm	65 (58 – 73)	65 (59 – 72)	0.88
DBP rest, mmHg	78 (67 – 85)	78 (70 – 84)	0.58
SBP rest, mmHg	140 (124 – 154)	137 (126 – 151)	0.81
EF rest, %	61 (54 – 67)	65 (58 – 70)	<0.001
WMSI rest	1.0 (1.0 – 1.12)	1.0 (1.0 – 1.0)	<0.001
B lines rest, number*	0 (0-0); (0-11)	0 (0-0); (0-8)	0.02
LAD rest velocity, cm/s	29 (23 – 34)	24 (21 – 27)	<0.001
HR peak, bpm	122 (99 – 132)	130 (110 – 136)	0.01
DBP peak, mmHg	73 (65 – 83)	76 (69 – 85)	0.07
SBP peak, mmHg	136 (119 – 157)	139 (124 – 160)	0.06
EF at peak, %	65 (60 – 71)	69 (64 – 73)	0.001
WMSI at peak	1.0 (1.0 – 1.18)	1.0 (1.0 – 1.0)	<0.001
B lines peak, number*	0 (0-0); (0-14)	0 (0-0); (0-8)	0.04
LVCR	1.38 (1.06 – 1.89)	1.52 (1.28 – 1.97)	0.02
LAD peak velocity, cm/s	45 (37 – 54)	60 (52 – 70)	<0.001
CFVR	1.667 (1.452- 1.818)	2.4 (2.169- 2.75)	<0.001
HRR	1.785 (0.45)	1.872 (0.466)	0.08
ΔWMSI	0 (0-0); (-1.0 – 0.24)	0 (0-0); (-0.5 – 0.24)	0.09

CFVR- coronary flow velocity reserve, DPB- diastolic blood pressure, EF- ejection fraction, HR- heart rate, HRR- heart rate reserve (HR peak/HR rest ratio), LAD- left anterior descending coronary artery, LVCR- left ventricular contractile reserve (Force at peak/Force rest ratio; Force = SBP/LVESV, LVESV left ventricular end-systolic volume), SBP- systolic blood pressure, SE-

stress echocardiography, WMSI- wall motion score index, ΔWMSI- delta of wall motion score index (difference between peak and rest WMSI).

Table S3. Comparison between groups with confirmed left anterior descending coronary artery stenosis (LAD) > 70%, without LAD stenosis in the coronary angiography and after stents implantation or surgical revascularisation of LAD.

* $P < 0.05$, ** For B-lines median, IQR, minimal and maximal values were presented.

Variable	**Group 1, with LAD stenosis, n = 15**	**Group 2, without LAD stenosis, n = 75**	**Group 3 revascularized LAD, n = 40**	***P* value Group 1 vs 2**	***P* value Group 2 vs 3**	***P* value Group 1 vs 3**
Age, years	68 (61 – 74)	69 (64 – 74)	70 (63 – 77)	0.74	0.54	0.47
BMI, kg/m^2	23 (22 – 29)	27 (25 – 30)	29 (27 -31)	0.06	0.18	0.02
HR rest, bpm	68 (61 – 70)	64 (58 – 71)	61 (58 – 69)	0.42	0.48	0.16
DBP rest, mmHg	73 (63 – 80)	76 (65 – 84)	80 (73 – 86)	0.19	0.1	0.02
SBP rest, mmHg	124 (119 – 141)	140 (128 – 151)	146 (131 – 159)	0.02	0.22	0.01
EF rest, %	46 (33 – 64)	61 (55 – 68)	62 (52 – 68)	0.006	0.75	0.009
WMSI rest	1.41 (1.02 – 1.75)	1.0 (1.0 – 1.12)	1.0 (1.0 – 1.21)	<0.001	0.05	0.012
B lines rest, number **	0.0 (0.0 – 0.75); (0 - 4)	0.0 (0.0 – 0.0); (0 - 9)	0.0 (0.0 – 0.0); (0 – 7)	0.17	0.63	0.42
LAD rest velocity, cm/s	29 (23 – 43)	26 (22 – 32)	26 (22 – 33)	0.32	0.94	0.3
HR peak, bpm	127 (89 – 135)	124 (95 – 133)	125 (107 – 133)	0.69	0.75	0.9
DBP peak, mmHg	72 (60 – 82)	72 (65 – 85)	79 (70 – 90)	0.58	0.11	0.13
SBP peak, mmHg	128 (112 – 146)	135 (122 – 158)	143 (123 – 161)	0.29	0.47	0.15
EF at peak, %	51 (36 – 59)	67 (61 – 72)	67 (61 – 72)	<0.001	0.96	<0.001
WMSI at peak	1.41 (1.18 – 1.79)	1.0 (1.0 – 1.12)	1.06 (1.0 – 1.24)	<0.001	0.068	<0.001
B lines peak, number**	0.0 (0.0 – 0.0);(0 - 4)	0.0 (0.0 – 0.0); (0 - 4)	1.0 (0.0 – 2.0); (0 – 9)	0.87	0.14	0.44
LVCR	1.191 (0.89 – 1.394)	1.332 (1.157 – 1.978)	1.505 (1.133 – 1.792)	0.05	0.52	0.02
LAD peak velocity, cm/s	50 (34 – 65)	55 (42 – 64)	52 (41 – 63)	0.72	0.87	0.74
CFVR***	1.653 (1.36 – 1.897)	2.057 (1.689 – 2.437)	1.972 (1.648 – 2.372)	0.02	0.68	0.047
HRR	1.765 (0.447)	1.782 (0.433)	1.882 (0.464)	0.89	0.25	0.4
ΔWMSI	0 (0-0.105)	0 (0-0)	0 (0-0)	0.04	0.38	0.004

***numbers of feasible CFVR in the compared groups were: 10 vs 69 vs 39, respectively

CFVR- coronary flow velocity reserve, DPB- diastolic blood pressure, EF- ejection fraction, HR- heart rate, HRR- heart rate reserve (HR peak/HR rest ratio), LAD- left anterior descending coronary artery, LVCR- left ventricular contractile reserve (Force at peak/Force rest ratio; Force = SBP/LVESV, LVESV left ventricular end-systolic volume), SBP- systolic blood pressure, SE- stress echocardiography, WMSI- wall motion score index, ΔWMSI- delta of wall motion score index (difference between peak and rest WMSI).