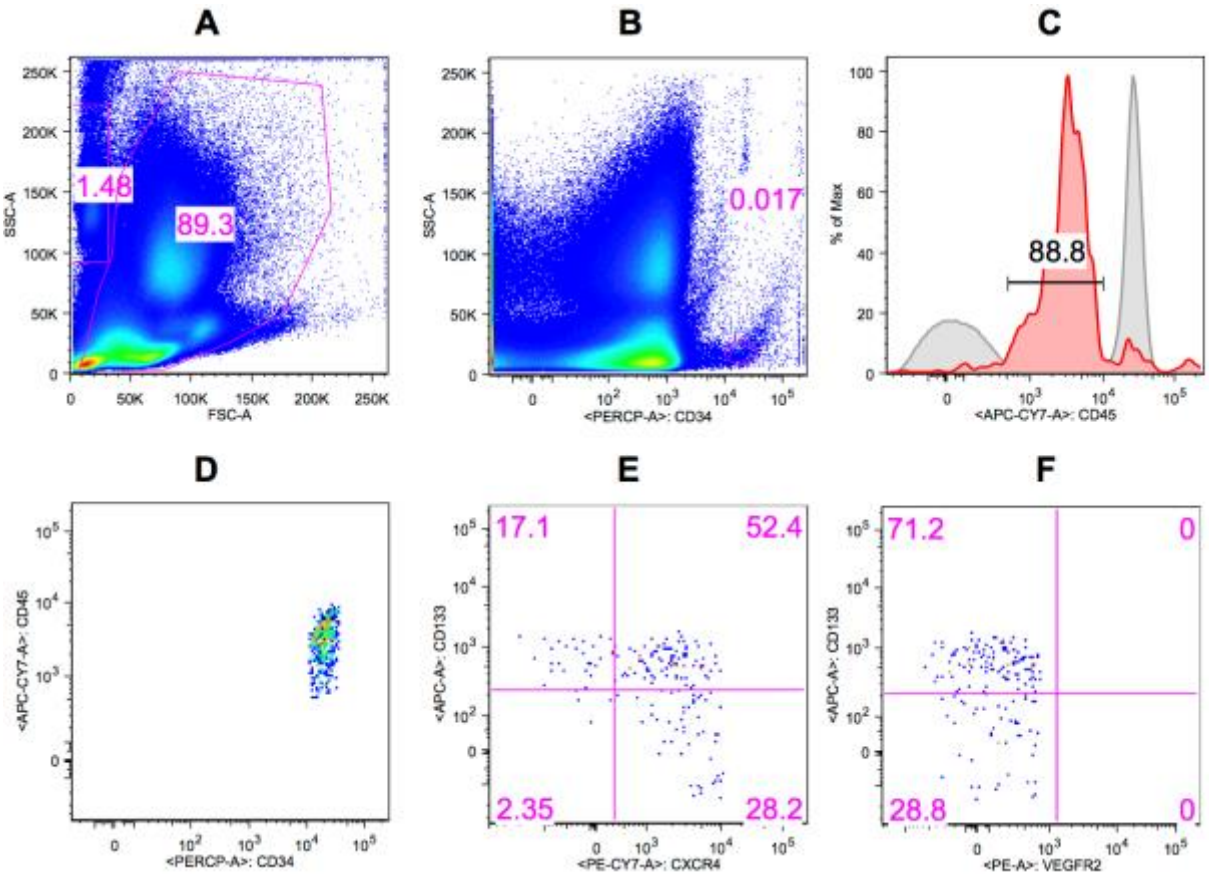
SUPPLEMENTAL MATERIAL.

Progenitor Cell Quantification by Flow Cytometry

Peripheral blood was collected in EDTA tubes and incubated with fluorochrome-labeled monoclonal antihuman mouse antibodies within 4 hours. Cell populations enriched for circulating PCs were enumerated using flow cytometry (**supplemental figure 1**) as CD45med cells co-expressing CD34+, CD133+, VEGFR2+, or CXCR4+. We incubated 300 µL of peripheral blood with 7 µL of FITC-CD34 (BD Biosciences), PerCP-CD45 (BD Biosciences), PE-VEGFR2 (R&D system) and 5 µL APC-CD133 (Miltenyi), and 3ul PE-Cy7-conjugated anti-CXCR4 (EBioscience, clone 12G5) in the dark for 15 minutes. Then 1.5 mL ammonium chloride lysing buffer was added to lyse red blood cells[1, 2]. 1.5 mL staining medium (PBS with 3% heat-inactivated serum and 0.1% sodium azide) was added to stop the lysing reaction. Prior to flow cytometry, 100 µL of ccuCheck Counting Beads (Invitrogen, Cat#: PCB100) were added to act as an internal standard for direct estimation of the concentration of target cell subsets. At least 2.5 million events were acquired from the cytometer. Flow data were analyzed with Flowjo software (Treestar, Inc.). Absolute mononuclear cell count was estimated as the sum of lymphocytes and monocytes using a Coulter ACT/Diff cell counter (Beckman Coulter). PC populations are reported as cell counts/mL. In 20 samples that were repeatedly analyzed on two occasions by the same technician, the coefficients of variation of the cell types were: CD34+ 2.9%; CD34+/CD133+ 4.8%; CD34+/CXCR4+ 6.5% and CD34+/CD133+/CXCR4+ 7.5%, CD34+/VEGFR2+ cells 21.6%. There were significant correlations between the progenitor cells subtypes, with moderate-strong correlations between CD34+, CD34+/CD133+, CD34+/CXCR4+ (r range 0.75-0.91, $P<0.001$), and weak correlations (r range 0.12-0.34, $P<0.001$) between CD34+/VEGFR2+ subtypes and the aforementioned PCs.

Supplementary Figure 1.

Flow Cytometry analysis of blood progenitor cells. Panel A: forward scatter and side scatter gates following lyse-no wash of blood and the Addition of fluorescent counting beads. Panel B: gating of CD34+, low side scatter cells from blood leukocytes shown in panel A. Panel C: histograms of CD45 expression in the CD34+ low side scatter cells (red histogram) shown in panel B or the CD34- cells (grey histogram). Panel D: the pattern of co-expression of CD34 and CD45dim on blood progenitors shown on panel C. Panel E: the co-expression of CD133 and CXCR4 on CD34+CD45dim blood progenitors shown on panel C. Panel F: the co-expression of CD133 and VEGFR2 on CD34+CD45dim blood progenitors shown on panel C.



Supplementary table 1. Relationship between progenitor cells and patient characteristics

	CD34		CD34/CD133		CD34/VEGF		CD34/CXCR4	
	rho	p value	rho	p value	rho	p value	rho	p value
Male	0.07	0.10	0.02	0.66	0.14	0.002	0.09	0.04
Black	0.01	0.82	0.05	0.23	0.01	0.91	0.03	0.45
Smoking	-0.01	0.86	-0.01	0.85	-0.11	0.01	0.00	0.92
Age	-0.19	<0.001	-0.24	<0.001	-0.002	0.97	-0.13	0.003
Body mass index	0.10	0.02	0.12	0.01	-0.01	0.88	0.05	0.23
Diabetes	0.08	0.08	0.09	0.04	-0.14	0.002	0.03	0.52
Hypertension	-0.09	0.05	-0.11	0.01	-0.03	0.58	-0.05	0.30
Hyperlipidemia	-0.004	0.93	-0.01	0.79	0.00	0.95	0.04	0.40
Estimated GFR	0.10	0.02	0.08	0.09	0.07	0.10	0.08	0.06

Supplemental table 2. Baseline characteristics for Mental Stress Ischemia Prognosis Study (MIPS) study

Variable	
Male n (%)	443 (76.1)
Age, years man (SD)	63.1 (9.2)
Body Mass Index kg/m2 mean (SD)	29.7 (5.3)
Black n (%)	153 (26.3)
Smoking n (%)	347 (59.8)
Diabetes n (%)	186 (32)
Hypertension n (%)	475 (81.6)
Hypercholesterolemia n (%)	107 (18.4)
Estimated GFR mL/min/1.73 m2 mean (SD)	78.5 (18.7)
Ejection fraction% mean (SD)	48.7 (15.5)
ACE/ARB use n (%)	365 (62.7)
Aspirin use n (%)	503 (86.6)
Plavix use n (%)	197 (33.9)
Statin use n (%)	494 (85.3)
Beta Blocker use n (%)	437 (75.2)
Obstructive CAD n (%)	539 (92.6)
History of myocardial infarction n (%)	208 (35.7)
History of CABG n (%)	195 (33.5)
History of PCI n (%)	321 (55.2)
Heart failure with preserved ejection fraction	60 (35.5)
Heart failure with reduced ejection fraction	109 (64.5)
CD34+ cell/mL median (IQR)	1609 (1020-2419)
CD34+/CD133+ cell/mL median (IQR)	733 (451-1122)
CD34+/CXCR4+ cell/mL median (IQR)	655 (364-1043)

Supplemental table 3. Validation in the Mental Stress Ischemia Prognosis Study (MIPS) cohort

Cell populations*	No heart failure (n=445)	Heart failure (n=137)	P-value
CD34+	1648 (1074-2446)	1395 (884-2193)	0.02
CD34+/CD133+	766 (466-1138)	659 (411-1070)	0.07
CD34+/CXCR4+	680 (388-1096)	564 (312-903)	0.005

*Cell/mL median IQR)

Supplementary table 4. Relationship between progenitor cells and echocardiogram parameters

	CD34		CD34/CD133		CD34/VEGF		CD34/CXCR4	
	rho	p value	rho	p value	rho	p value	rho	p value
Right Ventricular systolic pressure	-0.15	0.004	-0.16	0.003	-0.06	0.28	-0.11	0.03
Left ventricular internal diameter end diastole	0.07	0.18	0.08	0.13	0.09	0.08	0.09	0.08
Left ventricular internal diameter end systole	0.01	0.91	0.004	0.94	0.04	0.39	0.03	0.60
Interventricular septal end diastole	-0.01	0.77	-0.01	0.88	0.003	0.95	-0.003	0.95
Left ventricular posterior wall end diastole	-0.01	0.80	-0.01	0.88	-0.04	0.42	-0.01	0.88

References:

1. Duda DG, Cohen KS, Scadden DT and Jain RK. A protocol for phenotypic detection and enumeration of circulating endothelial cells and circulating progenitor cells in human blood. *Nat Protoc*. 2007;2:805-10.
2. Mahar EA, Mou L, Hayek SS, Quyyumi AA and Waller EK. Flow cytometric data analysis of circulating progenitor cell stability. *Data Brief*. 2017;10:346-348.