Plaque Burden vs. Plaque Composition

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Disclosures

• None
Background

Why Is Subclinical Disease Superior to Risk Factor Assessment?

- Integration of Risk Factors including Unknown Factors, Multiple SNPs
- Subclinical Disease Reflects “Dosage” of Risk Factor over time
- Subclinical Disease Reflects the High Risk Patient-the vulnerable plaque does not

The Courage Trial-Stents vs. Medical Therapy

Hazard ratio: 1.01; 95% CI: (0.84-1.37); P=0.56

- No. at Risk
- PCI: 1138 1127 1115 1097 1077 1057 1035 1015 995 976 956 933 910 887 864 841 818 795 772 749 726 703 680 657 634 611 588 565 542 519 496 473 450 427 404 381 358 335 312 289 266 243 220 197 174 151 128

Survival Free of ACS: Hazard ratio: 1.01; 95% CI: (0.84-1.37); P=0.56

- PCI: 1138 1127 1115 1097 1077 1057 1035 1015 995 976 956 933 910 887 864 841 818 795 772 749 726 703 680 657 634 611 588 565 542 519 496 473 450 427 404 381 358 335 312 289 266 243 220 197 174 151 128
- Medical therapy: 1118 1106 1094 1082 1070 1058 1046 1034 1022 1010 998 986 974 962 950 938 926 914 902 890 878 866 854 842 830 818 806 794 782 770 758 746 734 722 710 698 686 674 662 650 638 626 614 602 590 578 566 554 542 530 518 506 494 482 470 458 446 434 422 410 398 386 374 362 350 338 326 314 302 290 278 266 254 242 230 218 206 194 182 170 158 156 154 152 150 148 146 144 142 140 138 136 134 132 130 128 126 124 122 120 118 116 114 112 110 108 106 104 102 100 98 96 94 92 90 88 86 84 82 80 78 76 74 72 70 68 66 64 62 60 58 56 54 52 50 48 46 44 42 40 38 36 34 32 30 28 26 24 22 20 18 16 14 12 10 8 6 4 2 0
Plaque Burden

Coronary Atherosclerosis is a Diffuse, Not a Focal Disease

Roberts WC. Am J Cardiol 1988;62; 142-143

Coronaries in Angina

Roberts WC Circulation 1976: 54(3) 388.
Diffuse CAD in Pts with AMI and CABG


Glagov S, NEJM 1987;316:1371-5

Figure 5. Diagram of Cross-Sectional Changes in Human Coronary Arteries. (Adapted from Glagov, S. in Atherosclerosis, 1987, by permission of the investigators and the publisher.)
Coronary Calcium as a Predictor of Coronary Events in Four Racial or Ethnic Groups (MESA)

Armin Arbab-Zadeh, Valentin Fuster,

The Myth of the “Vulnerable Plaque” Transitioning From a Focus on Individual Lesions to Atherosclerotic Disease Burden for Coronary Artery Disease Risk Assessment

Risk of Heart Attack vs. Extent of Atherosclerosis

Coronary Segments with Atherosclerosis

Cumulative Heart Attacks

John Gofman, Cardiology Digest February 1969: p.28-38

The Concept of Dose/Duration of Risk Factor Exposure
Conventional Approach—Ignores Duration of Risk Factor Exposure Past and Future

Hypercholesterolemia

Total Cholesterol Distribution: CHD vs Non-CHD Population

Framingham Heart Study—36-Year Follow-up

50% of CHD occurs in people with below average TC

Adapted from Castelli. Am J Cardiol. 1983;52(suppl):51-59.
Of 136,905 patients hospitalized with CAD, more than 75% had LDL levels below 130 mg/dl. Twenty-three percent had LDL-C ≤ 70 mg/dl. Most People who Develop Heart Attacks have “Normal” LDL Values.

Duration of LDL Exposure

Hyperlipidemia in Early Adulthood Increases Long-Term Risk of Coronary Heart Disease.
Hyperlipidemia in Early Adulthood Increases Long-Term Risk of Coronary Heart Disease – Where Statins not Recommended

Circulation 2015, 114: 1-20

JUPITER
Ridker et al NEJM 2009
Primary Trial Endpoint: MI, Stroke, UA/Revascularization, CV Death

Extended Statin Use
Effect of Long-Term Exposure to Lower LDL Beginning Early in Life on the Risk of CAD
A Mendelian Randomization Analysis

Ference BA. J Am Coll Cardiol 2012;60:2631–9

Sequence Variations in PCSK9, Low LDL, and Protection against Coronary Heart Disease


From Age 30-60s Patients Care About Lifetime Risk, Not 10 Year Risk

Is There a Role for Coronary Artery Calcium Scoring for Management of Asymptomatic Patients at Risk for Coronary Artery Disease?


Does the Extent of Atherosclerosis or the Rate of Atherosclerosis Predict Future Coronary Events? Percentile vs. Score

Detrano NEJM Volume 358:1336-1345

Why Do Coronary Events Occur Almost Exclusively After Extensive Atherosclerosis is Present?
The Role of Rheology

12
Rheology and Atherosclerosis

The role of shear stress in the pathogenesis of atherosclerosis

Cunningham, C. Laboratory Investigation (2005) 85, 9-23
Carotid Flow


Effects of Disturbed Flow on Vascular Endothelium

Physiol Rev 91: 327–387. 2011;
69 yo hypercholesterolemia
Disturbed Blood Flow Acutely Induces Activation and Apoptosis of the Human Vascular Endothelium

Thus, our findings raise the idea that disturbed blood flow induces EMPs which may further promote endothelial dysfunction at distal sites, resulting in a feed-forward vicious cycle of vascular injury.

Hypertension. 2013;61:615-621
Thus, our findings raise the idea that disturbed blood flow induces EMPs which may further promote endothelial dysfunction at distal sites, resulting in a feed-forward vicious cycle of vascular injury.

Jenkins NT, Hypertension. 2013;61:615-621
Steady Progression

Devereux Circulation, 1993

PQ
Conclusion

• Plaque Burden Trumps Plaque Composition

Thank You