Relation of Aspirin Response to Age in Patients with Stable Coronary Artery Disease

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Background

- The biologic response to aspirin therapy is not uniform; rather, there is wide variability between individuals in platelet-level responsiveness.
- The estimated prevalence of low response to aspirin is variable 5-45%, depending on the assay used, cutoff value chosen and population examined.
- Resistance to aspirin has been consistently associated with an increased risk of adverse clinical outcomes in patients with CAD and patients undergoing PCI.

Background

- Recent data have revealed reduced response to clopidogrel in older patients with CAD
- Despite the high rates of ischemic disease and bleeding events in this segment of the population, there are no established data regarding the proportion of aspirin low response rates in older adults

Aims

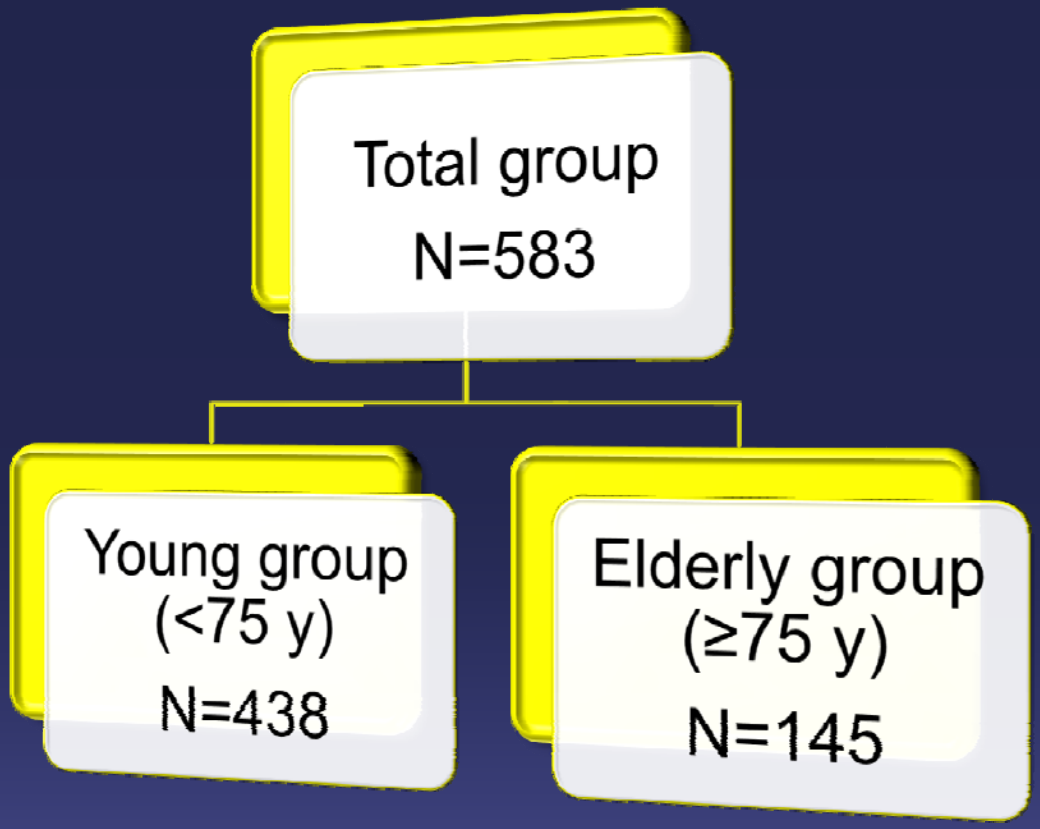
- To evaluate the response to aspirin among elderly (≥75 y) patients compared to younger (<75 y) patients with stable CAD.

Methods – *patients selection (1)*

- Study group included 585 outpatients, >18 yrs, with stable CAD, who were treated with aspirin for at least 1 week
  - CAD was defined as one of the followings: previous AMI, CABG, PCI, angiographic evidence of obstructive (≥50%) coronary disease.

- Exclusion criteria: PCI and/or ACS within 1 month of enrollment; concomitant treatment with NSAID or warfarin; thrombocytopenia, anemia; or renal insufficiency.

Methods – *patients selection (2)*



Methods – *platelet reactivity (1)*

- The VerifyNow Aspirin assay *(Accumetrics, San Diego, California)* was used to assess response to aspirin.

- Results are expressed as aspirin reaction units (ARU).
  - A cutoff of ≥500 ARU indicated resistance to the antiplatelet effects of aspirin.
  - This cutoff level has a sensitivity of 90% and specificity of 75% for identification of aspirin resistance when compared with AA-induced LTA

Methods – *blood sampling (2)*

- Turbidimetric platelet aggregation (LTA) was performed in a subgroup of 149 patients (25.6% of the study sample).
- Aggregation was performed in platelet-rich plasma in response to arachidonic acid
- The extent of aggregation was defined as the maximal light transmission ≤6 min after addition of the agonist

Results (1)

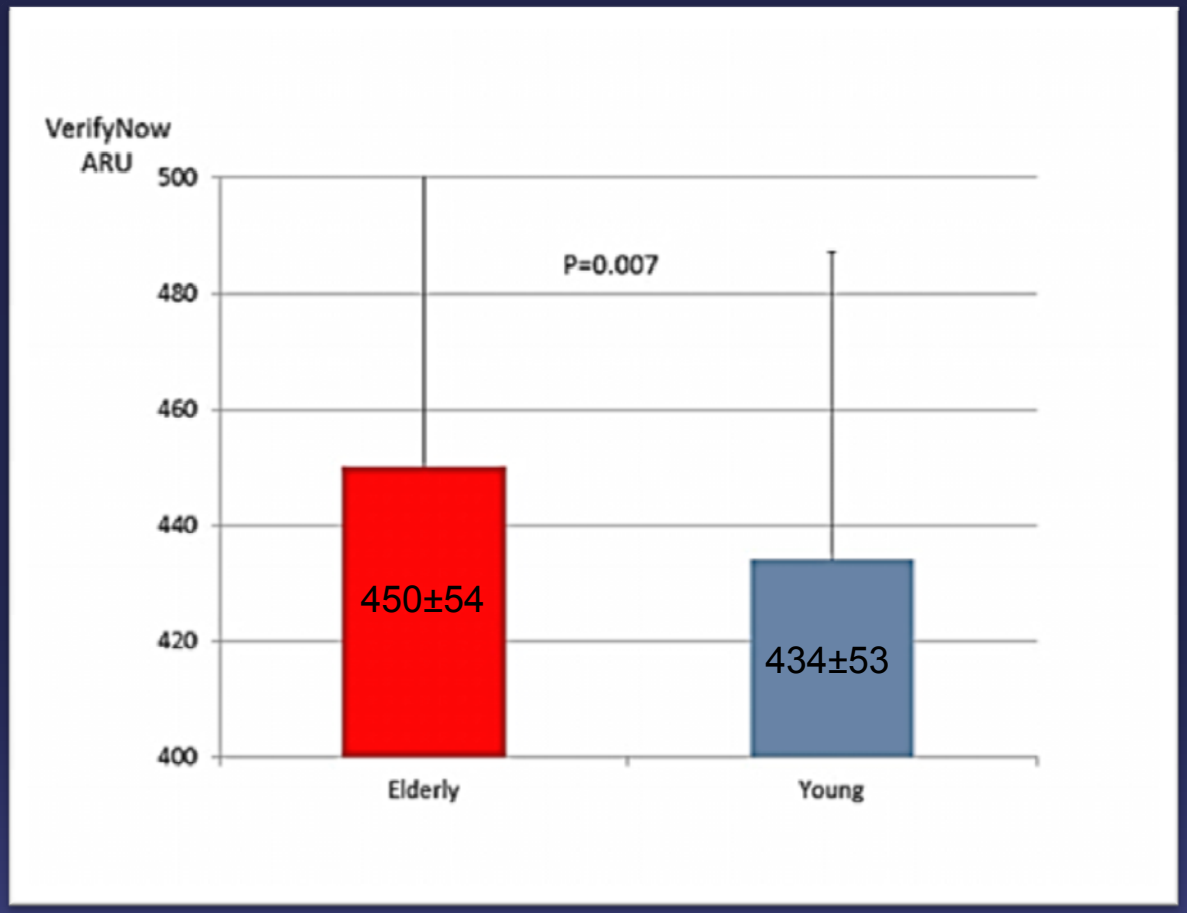
	Young Group (n=438)	Elderly Group (n=145)	*p* value
Age (years ± SD)	62±9	80±4	**<0.0001**
Men (%)	342 (78)	120 (83)	0.22
Body mass index (kg/m^2 ± SD)	29±12	26±4	**<0.0001**
Diabetes (%)	245 (40)	80 (38)	0.93
Hypertension (%)	129 (69)	34 (77)	0.17
Hyperlipidemia (%)	75 (80)	26 (78)	0.86
Current smoker (%)	44 (11)	13 (10)	0.3
Prior myocardial infarction (%)	205 (47)	76 (52)	0.28
Prior coronary artery bypass graft (%)	120 (27)	60 (41)	**0.002**
Prior PCI (%)	319 (73)	110 (76)	0.54

Results (2)

	Young Group (n=438)	Elderly Group (n=145)	*p* value
Aspirin 75-100 mg (%)	357 (82)	118 (81)	0.97
Aspirin 160-325 mg (%)	78 (18)	25 (17)	0.97
Clopidogrel	23 (5.3%)	5 (3.4%)	0.4
Statins (%)	376 (86)	120 (83)	0.58
Beta-blockers (%)	284 (65)	95 (66)	0.9
Angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers (%)	241 (55)	80 (55)	0.98
Calcium-channel blockers (%)	58 (13)	37 (26)	0.03

Results (3)

VerifyNow in elderly vs. younger patients



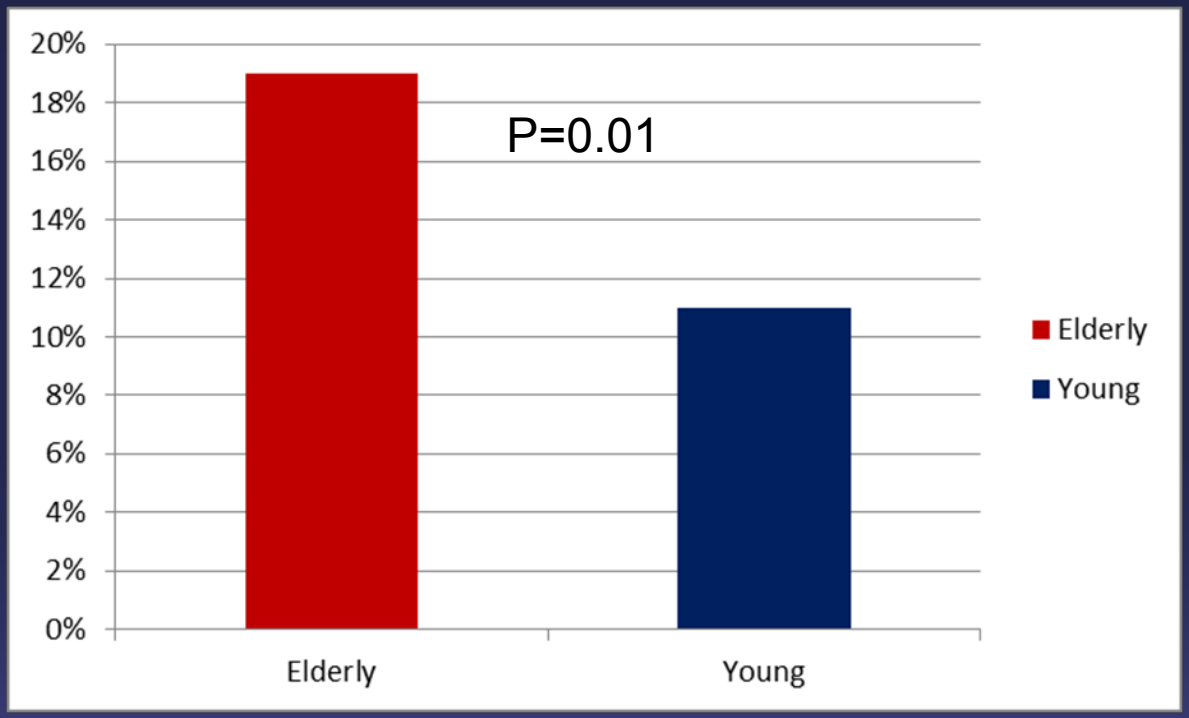
Age was found to be an independent predictor of VerifyNow scores (as a continuous variable) by multivariate linear regression model, adjusted for the primary covariates of gender, BMI and diabetes (P=0.007)

Results (4)

	Young Group (n=117)	Elderly Group (n=32)	*p* value
AA induced aggregation (%)	10.9±5.2	13.5±6	**0.03**
VerifyNow (ARU)	443±69	471±64	**0.04**

Among a subgroup of 149 patients which were also tested by LTA

Results (5)



Aspirin resistance rated according to ARU ≥500

Results (6)

Gender stratification of VerifyNow scores (ARU) in young and elderly patients

	Elderly Group	Young Group	p value
Total cohort (n)	450±54 (135)	434±53 (438)	**0.0007**
Men (n)	448±52 (121)	435±51 (343)	**0.02**
Women (n)	459±64 (24)	429±59 (95)	**0.048**
p value for men vs. women	0.45	0.35	

Main Findings

- Our study identified a reduction in aspirin responsiveness in relation to age.
- Elderly patients ≥75 yrs had higher platelet reactivity (VerifyNow scores) than younger patients < 75 yrs
- These results appeared to be consistent in both men and women.
- Our finding were also validated by higher AA-induced platelet aggregation values than in the younger cohort.

Conclusions

- Our study highlights the potential differences between young and elderly in response to aspirin, with elderly patients exhibiting higher residual platelet reactivity despite aspirin treatment.

- The clinical implications of our observation require further investigation.

Thank You