Οξύ Έμφραγμα του Μυοκαρδίου στους νέους

39-ο Πανελλήνιο Καρδιολογικό Συνέδριο

Αθήνα 18-20 Οκτωβρίου 2018

Βλάσης Ν. Πυργάκης  MD  FESC  FACC

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Γεν. Κρατ. Νοσοκομείου Αθηνών «Γ. ΓΕΝΝΗΜΑΤΑΣ»
definition of "young" patients with AMI

Most studies: **age cut-off**: 35 or 45 year of age
Prevalence of CHD by age and sex

National Center for Health Statistics and National Heart, Lung, and Blood Institute
Acute coronary syndromes in young patients: Presentation, treatment and outcome
Andreas W. Schoenenberger a,b, Dragana Radovanovic c, Jean-Christophe Stauffer d, Stephan Windecker e, Philip Urban f, Gregor Niedermaier g, Pierre-Frédéric Keller h, Felix Gutzwiller e, Paul Erne i,* and For the AMIS Plus Investigators

ABSTRACT

Background: Acute coronary syndromes (ACS) in very young patients have been poorly described. We therefore evaluate ACS in patients aged 35 years and younger.

Methods: In this prospective cohort study, 76 hospitals treating ACS in Switzerland enrolled 28,778 patients with ACS between January 1, 1997, and October 1, 2008. ACS definition included ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), and unstable angina (UA).

Results: 195 patients (0.7%) were 35 years old or younger. Compared to patients >35 years, these patients were more likely to present with chest pain (91.6% vs. 83.7%; P = 0.003) and less likely to have heart failure (Killip class II to IV in 5.2% vs. 23.0%; P < 0.001). STEMI was more prevalent in younger than in older patients (73.1% vs. 58.3%; P < 0.001). Smoking, family history of CAD, and/or dyslipidemia were important cardiovascular risk factors in young patients (prevalence 77.2%, 55.0%, and 44.0%). The prevalence of overweight among young patients with ACS was high (57.8%). Cocaine abuse was associated with ACS in some young patients. Compared to older patients, young patients were more likely to receive early percutaneous coronary interventions and had better outcome with fewer major adverse cardiac events.

Conclusions: Young patients with ACS differed from older patients in that the younger often presented with STEMI, received early aggressive treatment, and had favourable outcomes. Primary prevention of smoking, dyslipidemia and overweight should be more aggressively promoted in adolescence.
AMI in the young

uncommon entity but very important problem:

✓ devastating effect on the active lifestyle
✓ psychological effects
✓ ability to work
✓ financial constraints for the person and the family
  (the main income producer of the family)
PATHOGENESIS of ACS in young

✓ Atheromatous CHD
✓ Non-atheromatous CHD
✓ Hypercoagulable states
✓ substance misuse
The atheromatous process starts in early childhood

Association of coronary heart disease risk factors with microscopic qualities of coronary atherosclerosis in youth.


necropsy study
760 young patients (30 – 34 yrs) who died of various causes

advanced CHD: 20% of men
8% of women
The aetiology of atheromatous CHD

is linked to the **conventional risk factors** as in adults
A prospective study of >7000 men of mean age 27 years followed for an average of 31 years (47 CHD deaths)

The CHD mortality rates per 1000 person-years:

- No risk factors: 0.7
- 1 risk factor: 2.4
- 2 or more risk factors: 5.4
the most common and most modifiable risk factor in young patients

smoking rates among MI patients

young patients with MI  65 - 92 %
patients > 45 years  24 - 56 %

CORONARY RISK FACTORS

smoking

association of smoking and MI

“young” : (OR 3.33  99% CI, 2.86-3.87)

older     (OR 2.44  99% CI, 2.86-3.87)

smoking

CORONARY RISK FACTORS

POPULATION ATTRIBUTABLE RISK

- What proportion of the disease incidence in a total population can be attributed to a specific exposure?
- To know the PAR, we need to know
- incidence in total population = $q_{pop}$
- incidence in unexposed group (background risk) = $q -$

$$PAR = \left( \frac{q_{pop} - q -}{q_{pop}} \right) \times 100$$

$$q_{pop} = [q + \times p_e] + [q - \times (1 - p_e)]$$

$p_e$ → prevalence of exposure in total population.
$1 - p_e$ → prevalence of non-exposure.

• Reduction in incidence that would be observed if the population were entirely unexposed compared with the current exposure pattern

the PAR of smoking for MI among ‘‘young’’ men aged ♂<45 years

63.5% (95% CI, 42.0-80.6)

Family history of premature CVD in first-degree relatives, before 55 years of age in men and 65 years of age in women, increases the risk of CVD.


Family history of premature CAD in patients with AMI:
- young 41%
- middle aged 28%
- elderly 12%
Family history

“young” men aged < 45 years with a family history of MI:

the adjusted OR of MI 1.84 (95% CI, 1.07-3.17)

male gender

percentage of male gender in patients with AMI

< 45 years  90 %
older  68.4 %  (OR 3.59: 95% CI, 2.37-5.44)

AMIS Plus Study

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young patients compared to older:

- similar or lower total Cholesterol
- lower HDL (35 vs 43 mg/dL)
- higher triglycerides (239 vs 186 mg/dL)

(the most common lipid abnormality in young patients with MI)

Diabetes Mellitus

✓ incidence among “young” MI patients: 14.7%

✓ overall prevalence of DM among pts with ACS ≈ 45%

CORONARY RISK FACTORS

Diabetes Mellitus

the adjusted OR of MI among “young” men aged < 45 years with DM: 8.34 (95% CI, 1.67-41.6)


Young pts ( < 45 years) with MI without a history of DM:

65 % have impaired glucose tolerance
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autopsy study. 3000 persons 15-34 yrs who died from noncardiac causes

Increasing BMI was associated with fatty streaks and raised atherosclerotic lesions in coronary arteries of young men
Myocardial bridging can result in significant ischaemia during systolic contraction and can result in MI.

PCI and surgical splitting are more useful than medical management.
Spontaneous coronary artery dissection (SCAD) can occur in young adults.

OCT image showing false lumen with intramural hematoma

IVUS image showing false lumen with IMH
Spontaneous coronary artery dissection (SCAD)

- LAD is the culprit artery in most of cases
- previously believed to be very rare (0.2% to 1.1%)
- in modern series: the prevalence of SCAD in patients with ACS: 1.7% to 4%
- affects women in >90% of cases
- the prevalence of SCAD in young women with ACS: 22% to 43%
- accounts for 43% of pregnancy-related MI
RECREATIONAL DRUG USE

cocaine use

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Cocaine use

Accelerated Atherosclerosis

Hypertension

Thrombus Formation

Vasospasm

Cardiovascular Effects

Proarrhythmia
frequent Cocaine use accounted for 25% of nonfatal MI

RECREATIONAL DRUG USE

Cocaine use

in the UK:

✓ 4-fold increase in the number of cases of MI in cocaine users in the past 10 years


RECREATIONAL DRUG USE

Cocaine use

- cocaine effects can present up to 76 hours after its use

RECREATIONAL DRUG USE

Amphetamine

Marihuana

Binge drinking of alcohol

may be triggers of MI


Diagnostic CRITERIA FOR ANTIPHOSPHOLIPID SYNDROME (sydney revision)

- One clinical criterion
  - 1-Thrombosis
    Arterial Or Venous or Vasculopathy
  - 2-pregnancy morbidity
    a- 3 or more first trimester losses
    b- or 1 or more late fetal losses
    c- Or Severely preterm birth due to placental insufficiency

PLUS

- One laboratory criterion: persistent over 3 months
  - Lupus anticoagulant (present twice over 3 month) OR
  - Moderate/high titer IgG or IgM anticardiolipin OR
  - Moderate/high titer IgG or IgM anti-beta 2 glycoprotein I
Hypercoagulable States

Antiphospholipid syndrome

➢ often the disease of the young in their 30s

patients tend to have

➢ premature atherosclerosis and increased platelet adhesiveness
➢ recurrent episodes of thrombosis

1-Vascular thrombosis

- One or more clinical episodes of arterial, venous, or small-vessel thrombosis.
- Thrombosis may involve the cerebral vascular system, coronary arteries, pulmonary system (emboli or thromboses), arterial or venous system in the extremities, hepatic veins, renal veins, ocular arteries or veins, or adrenal glands.
Oral contraceptive pill use

primarily when combined with heavy smoking increases the risk of developing MI in young women

Kawasaki disease (KD)

Coronary vasculitis, leading to coronary aneurysm formation in 20 – 25% of untreated patients during the acute stage of the disease.

- Nearly half of acute aneurysms regress, but 20% lead to the development of coronary stenosis in the long term.
- Patients can present with MI or SCD.

“Strawberry tongue” of Kawasaki disease.
# AMIS Plus Study

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<td>Mean age ± SD, years</td>
<td>31.2 ± 2.8</td>
<td>65.8 ± 12.9</td>
<td>&lt;0.001</td>
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<tr>
<td>Female gender, % (no./no.)</td>
<td>14.9 (29/195)</td>
<td>27.7 (7931/28,583)</td>
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**Clinical presentation at admission**

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<td>Chest pain, % (no./no.)</td>
<td>91.6 (174/190)</td>
<td>83.7 (23,252/27,775)</td>
<td>0.003</td>
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<td>Dyspnea, % (no./no.)</td>
<td>12.8 (23/179)</td>
<td>26.8 (7074/26,408)</td>
<td>&lt;0.001</td>
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<tr>
<td>Killip class I, % (no./no.)</td>
<td>94.8 (181/191)</td>
<td>77.0 (21,741/28,218)</td>
<td>&lt;0.001</td>
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<td>Killip class II, % (no./no.)</td>
<td>3.1 (6/191)</td>
<td>15.9 (4488/28,218)</td>
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<tr>
<td>Killip class III, % (no./no.)</td>
<td>0.0 (0/191)</td>
<td>4.5 (1267/28,218)</td>
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<tr>
<td>Killip class IV, % (no./no.)</td>
<td>2.1 (4/191)</td>
<td>2.6 (722/28,218)</td>
<td></td>
</tr>
<tr>
<td>Cardio-pulmonary resuscitation, % (no./no.)</td>
<td>4.2 (8/189)</td>
<td>3.6 (1005/27,723)</td>
<td>0.560</td>
</tr>
<tr>
<td>STEMI, % (no./no.)</td>
<td>73.1 (141/193)</td>
<td>58.3 (16,613/28,501)</td>
<td>&lt;0.001</td>
</tr>
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<td>NSTEMI/UA, % (no./no.)</td>
<td>26.9 (52/193)</td>
<td>41.7 (11,888/28,501)</td>
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<td>Sinus rhythm, % (no./no.) d</td>
<td>97.3 (142/146)</td>
<td>91.0 (21,137/23,218)</td>
<td>0.005</td>
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<td>Atrial fibrillation, % (no./no.) d</td>
<td>0.7 (1/146)</td>
<td>5.2 (1216/23,218)</td>
<td>0.008</td>
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<td>Wide QRS complex tachycardia, % (no./no.) d</td>
<td>0.0 (0/146)</td>
<td>0.6 (146/23,218)</td>
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<td>ST-segment elevation, % (no./no.) d</td>
<td>73.1 (141/193)</td>
<td>54.5 (15,511/28,463)</td>
<td>&lt;0.001</td>
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<td>ST-segment depression, % (no./no.) d</td>
<td>15.8 (30/190)</td>
<td>25.3 (6913/27,337)</td>
<td>0.003</td>
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<td>Q waves, % (no./no.) d</td>
<td>20.7 (40/193)</td>
<td>18.8 (5365/28,462)</td>
<td>0.522</td>
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<td>T wave changes, % (no./no.) d</td>
<td>26.8 (51/190)</td>
<td>25.0 (6845/27,338)</td>
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<td>Left bundle branch block, % (no./no.) d</td>
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✓ A higher proportion of young patients do not report a history of previous angina
   (76% vs 49% in pts ≥60 years)

✓ in the majority of cases:
   an ACS that progresses rapidly to MI (most often an STEMI)
   if left untreated is the first manifestation of CHD

A potential diagnostic problem in younger subjects: myocarditis mimicking an AMI

78% of young patients with a clinical presentation of an ACS have a diffuse or focal myocarditis on myocardial imaging.


ANGIOGRAPHIC FINDINGS

less extensive disease in “young” MI patients than older pts

normal coronary arteries

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<td>younger</td>
<td>16%</td>
<td>21%</td>
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<td>older</td>
<td>2%</td>
<td>11%</td>
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ANGIOGRAPHIC FINDINGS

less extensive disease in “young” MI patients than older pts

1 vessel disease

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ANGIOGRAPHIC FINDINGS

less extensive disease in “young” MI patients than older pts

3 vessel disease

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</table>
the LAD artery is most commonly affected

Wolfe MW, Vacek JL. Myocardial infarction in the young. Angiographic features and risk factor analysis of patients with myocardial infarction at or before the age of 35 years. Chest 1988; 94:926.
Young patients with acute STEMI should be treated with primary PCI or, if not available, thrombolytic therapy. Reperfusion therapy is applied more often in young patients. Young patients do better than older patients regardless of the therapy received.
- reperfusion therapy is applied more often in young patients
- young patients do better than older patients regardless of the therapy received

Each increment of 10 years of age:
- increases the risk of death or re-infarction by 1.32

Patients are first stabilized with medical therapy and should undergo early coronary angiography and revascularization.

An early invasive strategy has been associated with improved survival regardless of age.

But
- this observation is based upon data from a study where the mean age of the invasive strategy cohort was 67 years.
- The efficacy of this strategy in patients < 40 years is uncertain (younger patients under-represented in the large clinical trials.)
Non-ST elevation MI


patients < 40 years, who had Cor Angio within 60 days of their first AMI

“routine coronary angiography post MI in those who are asymptomatic, aged 40 years or less and do not exhibit spontaneous or provicable post-infarction ischaemia is not warranted”

- controversial study published in 1994
- conducted over 24 years ago
Non-ST elevation MI

➢ current equipment, therapies and techniques afford better outcomes

➢ most cardiologists feel obligated to refer these patients for coronary angiography given their "young age" and the "need to know the coronary anatomy."

In a real-world setting

invasive management in “young” NSTEMI patients should be the norm rather than the exception
2018 ESC/EACTS Guidelines on myocardial revascularization

Invasive evaluation in Non-ST-Elevation Acute Coronary Syndromes

**Very High-Risk**
- Haemodynamic instability or cardiogenic shock
- Recurrent/ongoing chest pain refractory to medical txt
- Life-threatening arrhythmias or cardiac arrest
- Mechanical complications of MI
- Acute heart failure
- Recurrent dynamic ST-T wave changes

**High-Risk**
- Established diagnosis of non-ST-elevation myocardial infarction based on cardiac troponins
- Dynamic ST/T changes (symptomatic or silent)
- GRACE score >140

**Intermediate Risk**
- Diabetes mellitus or renal insufficiency
- LVEF <40% or congestive heart failure
- Early post-infarction angina or prior PCI/CABG
- GRACE risk score >109 and <140 or recurrent symptoms/ischaemia on non-invasive testing.

**Immediate Invasive (<2 hours)**
- IC

**Early Invasive (<24 hours)**
- IA

**Invasive (<72 hours)**
- IA
risk factor modification post-MI

smoking cessation

- 36% reduction in mortality
  (RR 0.64: 95% CI, 0.58-0.71)
- 49% reduction in coronary events recurrence
  (RR 1.51 (95% CI, 1.10-2.07)

## AMIS Plus Study

Acute coronary syndromes in young patients: Presentation, treatment and outcome

Andreas W. Schoenenberger \(^{1,2}\), Dragana Radovanovic \(^{3}\), Jean-Christophe Stauffer \(^{4}\), Stephan Windecker \(^{1}\), Philip Urban \(^{5}\), Gregor Niedermaier \(^{3}\), Pierre-Frédéric Keller \(^{1}\), Felix Gutzwiler \(^{1}\), Paul Erne \(^{1,5}\)

and For the AMIS Plus Investigators

<table>
<thead>
<tr>
<th>Patients with STEMI</th>
<th>Patients aged ≤35 years</th>
<th>Patients aged &gt;35 years</th>
<th>(P) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients with STEMI</td>
<td>142</td>
<td>16,613</td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary PCI(^{a}), % (no./no.)(^{c})</td>
<td>53.6 (75/140)</td>
<td>48.6 (8057/16,566)</td>
<td>0.270</td>
</tr>
<tr>
<td>Thrombolysis, % (no./no.)(^{c})</td>
<td>25.5 (36/141)</td>
<td>20.8 (3447/16,583)</td>
<td>0.174</td>
</tr>
<tr>
<td>Outcome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In-hospital mortality, % (no./no.)(^{c})</td>
<td>2.1 (3/142)</td>
<td>8.0 (1333/16,613)</td>
<td>0.005</td>
</tr>
<tr>
<td>MACE(^{b}), % (no./no.)(^{c})</td>
<td>2.9 (4/139)</td>
<td>10.4 (1689/16,274)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

## Patients with NSTEMI/UA

<table>
<thead>
<tr>
<th>Patients with NSTEMI/UA</th>
<th>Patients aged ≤35 years</th>
<th>Patients aged &gt;35 years</th>
<th>(P) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients with NSTEMI/UA</td>
<td>52</td>
<td>11,888</td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early PCI(^{a}), % (no./no.)(^{c})</td>
<td>59.6 (31/52)</td>
<td>34.5 (4087/11,836)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Any PCI(^{a}), % (no./no.)(^{c})</td>
<td>79.2 (38/48)</td>
<td>61.5 (6354/10,337)</td>
<td>0.013</td>
</tr>
<tr>
<td>Outcome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In-hospital mortality, % (no./no.)(^{c})</td>
<td>0.0 (0/52)</td>
<td>5.2 (622/11,888)</td>
<td>0.114</td>
</tr>
<tr>
<td>MACE(^{b}), % (no./no.)(^{c})</td>
<td>0.0 (0/52)</td>
<td>7.0 (812/11,666)</td>
<td>0.049</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>&lt; 40 years</th>
<th>&gt; 40 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>in hospital</td>
<td>0,7%</td>
<td>8,3%</td>
</tr>
<tr>
<td>6 months</td>
<td>3,1%</td>
<td>12%</td>
</tr>
</tbody>
</table>
Long-term outcome

Young patients have a good long-term outcome after MI


<table>
<thead>
<tr>
<th></th>
<th>young</th>
<th>older</th>
</tr>
</thead>
<tbody>
<tr>
<td>men</td>
<td>84%</td>
<td>75%</td>
</tr>
<tr>
<td>women</td>
<td>90%</td>
<td>77%</td>
</tr>
</tbody>
</table>

Survival rates at 7 years

No difference in the rate of reinfarction between younger and older men (18% vs 20%) and women (15% vs 21%)
Cumulative survival in patients <30 years presenting with acute coronary syndrome.

ATS = atherosclerosis; non-ATS = patients without angiographic evidence of atherosclerosis.
Long-term outcome

Beyond 10 years post-MI there is an alarming drop in survival among “young” MI patients

15 years mortality 25-29%


Long-term outcome

the rate of **sudden cardiac death** in “young” MI patients compared to the general population of a similar age

74-fold higher mortality

Long-term outcome

sudden cardiac death

The strongest independent risk factor:
LVEF < 45% (OR 4.4: 95% CI, 1.6-12.4)

heart failure post MI in young patients


improved acute management of MI

markedly reduced the rate of HF post MI the last decades

20% in 1970s
< 6% in 2005

➢ reduces mortality in patients aged <60 years
Percutaneous intervention


PCI in 89 patients ≤40 years  VS  1916 patients > 40 years of age

- periprocedural complications (death, MI, urgent CABG)
  0% vs 7%

After a 30 months follow-up:

- no death
- 5% required elective CABG
- 34% underwent repeat PCI for restenosis or disease progression

- easier to perform  (good physical condition, can better tolerate the stress of surgery and general anesthesia)
- no operative mortality
- rate of perioperative AMI  : 4%
- Survival rates  at 5 years  : 95%
  10 years  : 84 %
- no significant difference between the long-term patency rate of the SVG compared with other series that included older age groups
- The long-term patency was much higher with LIMA  grafts (93% versus 56 % with SVG)
Youth is not a time of life; it is a state of mind; it is not a matter of rosy cheeks, red lips and supple knees; it is a matter of the will, a quality of the imagination, a vigor of emotions; it is the freshness of the deep springs of life. Youth means a temperamental predominance of courage over timidity of the appetite, for adventure over the love of ease. This often exists in a man of 60 more than a boy of 20. Nobody grows old by merely a number of years. We grow old by deserting our ideals.

—Samuel Ullman, German-born Jewish-American poet and humanitarian

Youth

Samuel Ullman
(1840-1924)
written at the age of 78
Τα νιάτα δεν είναι περίοδος ζωής, είναι κατάσταση του νού. Δεν είναι κόκκινα μάγουλα, κόκκινα χείλη και ευλύγιστα γόνατα.

Είναι η επίκρατης της θέλησης, ιδιότητα της φαντασίας, δύναμη των αισθημάτων.

Είναι η επικράτηση του θάρρους απέναντι στην ατολμία, της επιθυμίας για περιπέτεια απέναντι στην απραξία.

Πιο συχνά την βρίσκεις σε έναν εξηντάρη από το ένα παιδί 20 ετών.

Κανένας δεν γερνάει μόνο και μόνο επειδή πέρασαν μερικά χρόνια.

Γερνάμε όταν λιποτακτούμε από τα ιδανικά μας..»
Jenifer Lopez

18 yrs

45 yrs