Editorial

Interventional Cardiology

Mortality in acute coronary syndromes: many small steps in the right direction

> "...there is more work to be done in refining percutaneous intervention and pharmaceutical treatments to improve survival in acute coronary syndromes."

Keywords: acute coronary syndrome • mortality • non-ST-segment myocardial infarction • ST segment elevation myocardial infarction • unstable angina

"*It is better to make many small steps in the right direction than to make one great leap forward only to stumble backward.*"

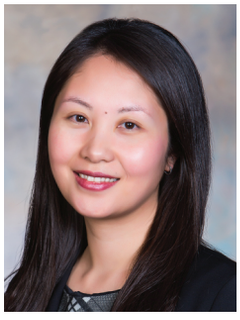
– Old Chinese proverb.

Technological and pharmacological advances in the treatment of acute coronary syndromes (ACS) have resulted in a worldwide decrease in morbidity and mortality after a myocardial infarction. Prior to the advent of percutaneous coronary intervention (PCI) in the 1980s, patients with ACS were placed on bed rest as the infarct completed it course. Fifty years later, patients now have invasive and pharmacological therapies that promise symptom relief, and improved morbidity and mortality. Overall, the primary goal is, and has always been, to improve survival. Unfortunately, data on mortality is oftentimes unclear, as mortality is commonly combined with other primary end points, such as major adverse cardiovascular events. The following is a brief summary of therapies, which have been shown to improve survival in patients with ACS.

Timely reperfusion for patients presenting with a ST segment elevation myocardial infarction (STEMI) or high-risk non-STEMI (NSTEMI) is now the standard of care in PCI-capable facilities, as it has been shown to improve survival. In patients with STEMI, a door-to-balloon time of less than 90 min has been shown to have lower mortality compared with a door-to-balloon time greater than 90 min (3.7 vs 7.3%, respectively; $p < 0.001$) [1]. Data has also shown that a reduction in door-to-balloon time to less than 60 min does not further improve survival [1]. One possible explanation for such a phenomenon is that the delay from the onset of ACS to first medical contact is a larger contributor to total ischemic time, as compared with door-to-balloon time.

Further refinements in technical aspects at the time of cardiac catheterization have also been shown to improve survival. In the HORIZONS-AMI study, overall mortality was lower for patients with STEMI who received bivalirudin monotherapy during primary PCI when compared with heparin plus a GPIIb/IIIa inhibitor (5.9 vs 7.7%, respectively; $p = 0.03$) [2]. One drawback of using bivalirudin is the increased rate of stent thrombosis in the first 24 h postintervention. But perhaps with the development of new antiplatelet agents with a faster therapeutic onset, the risk of stent thrombosis would be further reduced. A randomized controlled trial comparing bivalirudin monotherapy versus heparin monotherapy for primary PCI in combination with prasugrel would be a useful study. The use of GPIIb/IIIa inhibitors routinely with heparin has since fallen out of favor, secondary to increased bleeding risk.

The RIVAL trial demonstrated that radial access for patients with STEMI undergoing primary PCI resulted in lower mortality as compared with patients who underwent femoral access (1.3 vs 3.2%, respectively; $p = 0.006$) [3]. Worldwide, interventional cardiology training programs are recognizing the importance of training fellows to perform radial interventions. Deriving mortality benefit from radial interventions in STEMI is dependent upon the skill of the primary operator. In STEMI, radial access adds approximately



Grace Huang
University of Southern California, Keck School of Medicine, 1510 San Pablo Street, Suite 322, Los Angeles, CA 90033, USA

Leonardo Clavijo
Author for correspondence:
University of Southern California, Keck School of Medicine, 1510 San Pablo Street, Suite 322, Los Angeles, CA 90033, USA
Tel.: +1 323 442 6130
Fax: +1 323 442 6133
lclavijo@usc.edu

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2 min to the door-to-balloon time, as compared with femoral access [4].

The TAPAS trial showed that cardiac mortality was lower in patients who underwent aspiration thrombectomy compared with conventional treatment (3.6 vs 6.7%, respectively; p = 0.02) [5]. The use of more aggressive thrombectomy technology, such as the Angiojet® (Bayer, Leverkusen, Germany), has not been shown to improve survival.

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Pharmacological treatment has also been shown to improve survival in patients with ACS. Only three antiplatelet agents, aspirin [6], clopidogrel [7] and ticagrelor [8], have been shown to have mortality benefit. In addition, the mortality benefit of dual antiplatelet therapy is maximized when it is initiated upstream or prior to arrival in the cardiac catheterization laboratory [9]. The mortality benefit of β-blockers and angiotensin-converting enzyme inhibitors is derived when treatment is initiated within 24 h of presentation or prior to discharge, as long as patients do not have contraindications or relative contraindications to these classes of drugs. For patients with low systolic ejection fraction or heart failure, eplerenone given within 7 days postmyocardial infarction has been shown to reduce mortality (11.5 vs 16.1%; p < 0.0001) [10]. Lastly, intensive LDL-lowering therapy with atorvastatin has been shown to decrease mortality (8.3 vs 10.0%; p = 0.06) [11]. Although all of the above medications have been shown to improve survival, they also have potentially intolerable or life-threatening side effects. In addition, medication compliance becomes a problem with increasing number of drugs prescribed.

Despite such an armamentarium of invasive and pharmacological therapies that have been shown to reduce mortality in patients with ACS, mortality rates remain high. We have come a long way from the days of bed rest for the treatment of myocardial infarction; many steps in the right direction have been taken, but there is more work to be done in refining percutaneous intervention and pharmaceutical treatments to improve survival in ACS.

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