

Acute coronary syndromes: exploring the best way forward in optimising care

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To decrease overall mortality, we need to focus on maximising appropriate medical therapies

Increasing attention is being given to assessing and improving the quality of care of patients presenting with acute coronary syndromes (ACS).^{1,2} In this issue of the Journal (page 691), Chew and colleagues report on the use and survival impact of early invasive management (coronary angiography and revascularisation) in 3393 patients with ACS enrolled in the Australian prospective ACACIA (Acute Coronary Syndrome Prospective Audit) registry.³ They used propensity-adjusted regression modelling to quantify effects of invasive care independently of other confounders such as patient characteristics, contraindications to invasive care and use of pharmacological treatments. While rates of invasive care appeared near to optimal (90%) in patients with ST-segment-elevation myocardial infarction (STEMI), rates were purported to be less optimal in those with non-STEMI (71%) and unstable angina (45%).

The study is unique in showing a 47% reduction in all-cause death at 1 year as a result of early invasive care, a finding used to argue for a greater use of this approach across the spectrum of ACS. The magnitude of this treatment effect is at odds with systematic reviews of randomised trials which report that survival benefits are restricted to patients with STEMI undergoing primary angioplasty, with relative risk reduction of death (compared with thrombolysis) no more than 32%.⁴ Such patients represented just over a fifth of the patients evaluated in ACACIA. In contrast, contemporary trials of routine invasive care versus medical therapy in patients with non-ST-segment elevation ACS (NSTEMACS), who comprised three-quarters of the cohort, show no conclusive mortality benefit, although reinfarction and anginal burden are significantly reduced.⁵ Separate analyses for patients with STEMI versus those with NSTEMACS were not reported, which brings into question the validity of implying that greater use of an invasive strategy among all patients with ACS would translate into proportionately more survival benefit. The authors argue that their cohort included many high-risk patients who tend to be excluded from trials, and among whom they infer a survival benefit was achieved.

Several issues warrant consideration. Can observational studies validly show treatment benefits not seen in randomised trials? How replicable are these effects? If such an effect is real, would the number of lives saved from optimising invasive care exceed that achieved from optimising other forms of care, thus serving as a quality improvement priority? If so, what might be the most effective optimisation strategies?

Even the best observational design can be biased by prognostically important baseline differences among patients, often because of unobserved or unreported treatment selection biases. Chew et al did their best to minimise such bias by estimating the likelihood (or propensity) of patients to receive invasive care on the basis of patient characteristics ascertained *before* such treatment was given. The association between invasive care and 12-month mortality was then assessed with regression modelling that adjusted for variables known or thought highly likely to influence mortality, including

medical therapies such as statins and angiotensin-converting enzyme (ACE) inhibitors — although antiplatelet agents and β -blockers were notably absent. This association was then further adjusted after inserting the propensity score as a continuous variable.

Unfortunately, methodological concerns persist for several reasons. First, the literature is replete with high-profile examples of well performed observational studies (eg, hormone replacement therapy and cardiovascular mortality, β -carotene and cancer prevention) suggesting favourable treatment effects that were later dismissed or reversed in large, pragmatic randomised trials. Second, different observational studies, which have included analytical methods other than propensity scoring, give very different results. An American study showed that early coronary angiography for acute myocardial infarction (AMI) was associated with a 50% reduction in mortality at 7 years using propensity analysis (designed to control for overt bias), but this fell to a 16% decrease when instrumental variable analysis was used (designed to control for hidden bias as well).⁶ A propensity-adjusted analysis of French patients with STEMI presenting to interventional versus non-interventional hospitals (the former highly correlated with higher rates of invasive care) revealed only a 24% decrease in mortality at 1 year.⁷ Third, the most appropriate design for observational studies remains unclear, with some arguing propensity scoring is no better than traditional multivariate regression adjustment.⁸ Fourth, as propensity analysis cannot adjust for unmeasured characteristics, sensitivity analyses are recommended to gauge effects of potential confounders which, for invasive care in ACS, may include patients' socioeconomic status.⁹ Finally, trials of invasive care may actually overestimate treatment effects achievable in routine practice given the expertise, logistical support and rapid institution required for the optimal results available in high-volume research centres.

With regard to prioritising efforts at improving quality of care, the use of early invasive care in patients with STEMI in the study by Chew et al was in accordance with trials and guidelines. In contrast, within the total cohort, there was considerable underuse of key drugs at discharge and at 12 months, respectively: β -blockers, 68% and 57%; aspirin, 87% and 74%; statins, 82% and 72%; ACE inhibitors or angiotensin receptor antagonists, 67% and 64%. This underuse was most pronounced in patients not receiving invasive care and, by association, not admitted to a metropolitan centre. Of all AMI-related deaths that are prevented by therapeutic interventions, both acutely and as secondary prevention, medical treatments account for 80% of these (35% acutely, 45% secondarily) compared with only 6% for early invasive management.¹⁰ If all indicated drugs are prescribed to eligible patients, risk-adjusted mortality at 6 months is reduced by 90% compared with patients who receive none of these drugs.¹¹ Routine use of more costly invasive care is not associated with population survival benefit beyond that seen with optimal medical

management.¹² Thus, if decreasing overall mortality is the aim, a focus on maximising administration of appropriate medical therapies across all hospitals should take precedence over extending invasive care to all or most patients with ACS, especially as there are low-cost interventions that can increase rates of prescribing at discharge up to 90%.¹³

This is not to say the delivery of timely invasive intervention, particularly to patients presenting to non-interventional hospitals, is unimportant given its mortality benefit in STEMI⁴ and morbidity reduction in high-risk NSTEMI.⁵ There are actionable strategies for improving region-wide access to intervention¹⁴ and reducing door-to-balloon times¹⁵ for patients with acute STEMI, and these deserve consideration in Australian settings. Risk stratification methods for identifying patients with NSTEMI who are most in need of referral to interventional centres¹⁶ require universal implementation. More globally, quality improvement strategies — comprising use of opinion leaders and educational outreach, guideline-based decision support tools, regular audit and feedback, and clinical process redesign — have been validated in the management of patients with ACS,¹⁷ and innovative, multidisciplinary programs that integrate multiple strategies need to be maintained. What is critical is the continuance of well designed prospective registries like ACACIA, which provide standardised and representative data that allow us to monitor the quality of care and the effects of whatever actions we may take towards improving it.

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