Discordance between level of risk and intensity of evidence-based treatment in patients with acute coronary syndromes

Ian A Scott, Patrick H Derhy, Di O'Kane, Kylie A Lindsay, John J Atherton, Mark A Jones for the CPIC Cardiac Collaborative

ABSTRACT

Objectives: To examine the relation between treatment intensity and level of risk in routine hospital care of patients with acute coronary syndromes (ACS), and to identify independent predictors of use or omission for each of eight evidence-based treatments.

Design: Retrospective cohort study of patients fulfilling case definition for ACS in whom absolute risk of adverse outcomes was quantified (as low, moderate, or high risk) using formal prediction rules, and for whom treatment eligibility was determined using expert-agreed criteria.

Participants and setting: 3912 consecutive or randomly selected patients admitted to 21 hospitals in Queensland, Australia between 1 August 2001 and 31 December 2005.

Results: The proportions of eligible patients receiving treatment varied inversely with risk level in regard to reperfusion therapies of fibrinolytic therapy or primary angioplasty (low risk, 88.3%; moderate risk, 61.9%; high risk, 18.2%; $P < 0.001$), heparin (91.4%; 83.7%; 72.8%; $P < 0.001$) and early invasive intervention (33.6%; 24.0%; 18.5%; $P < 0.001$). Significantly more low- and moderate- than high-risk patients received β-blockers (87.0%; 88.5%; 79.1%; $P < 0.001$), lipid-lowering agents (87.3%; 84.8%; 65.8%; $P < 0.001$), and referral to cardiac rehabilitation (51.8%; 46.0%; 34.4%; $P < 0.001$) at discharge. The most frequent independent predictors of treatment omission in all patients included increasing age (5 of 8 treatments), previous ACS or atrial tachyarrhythmias (4 of 8), and past history of cerebrovascular accident or congestive heart failure (3 of 8).

Conclusion: In routine care of ACS, eligible patients at high risk receive treatment less frequently than those at low and moderate risk. Reforms in professional education, routine use of risk stratification tools, guideline recommendations tailored to population-specific reductions in absolute risk, and better hospital networking with standardised triage and referral procedures for invasive procedures may help reduce selection bias in the delivery of indicated care.

MJA 2007; 187: 153–159

In Australia, about 100 000 patients are hospitalised each year with acute coronary syndromes (ACS)[1] — either unstable angina (UA) or acute myocardial infarction (AMI) of non-ST-elevation (NSTEMI) or ST-elevation (STEMI) type. Changing diagnostic criteria, the advent of sensitive troponin assays, and an ageing population are causing ACS incidence to rise worldwide.[2,3] Effective treatments include reperfusion therapy, heparin, early invasive intervention (coronary angiography and revascularisation by percutaneous coronary intervention [PCI], as indicated), antiplatelet agents (aspirin and/or clopidogrel), β-blockers, angiotensin-converting enzyme inhibitors or angiotensin II receptor antagonists, lipid-lowering agents, and cardiac rehabilitation. Large-scale quality improvement programs have attempted to optimise in-hospital use of these treatments among eligible patients.[4-7]

Patients at highest absolute risk of death or coronary events would be expected to derive greater benefit from treatment than lower-risk patients.[8] Accordingly, the propensity to administer therapies should be greatest in such individuals. However, registry data show that high-risk but eligible elderly patients are less likely than younger patients to receive fibrinolytic therapy, invasive interventions, aspirin, β-blockers, or statins.[9,10] A similar pattern is seen in high-risk patients with diabetes[11] or renal insufficiency.[12] Even among patients with above average risk, rates of statin use are lowest among patients with highest mortality risk,[13] and similar patterns are seen among patients undergoing coronary revascularisation.[14]

We sought to determine the relation between level of risk and frequency of administration of specific therapies; and to identify clinical and system-of-care factors which predict greater or lesser use of specific treatments among all eligible patients.

METHODS

Participants

Patients were those registered with the Queensland Clinical Practice Improvement Centre (CPIC) Cardiac Collaborative between 1 August 2001 and 31 December 2005. Data on baseline clinical characteristics, use of interventions, in-hospital course and eligibility criteria for specific treatments (available on request and at http://www.qheps.health.qld.gov.au/cpic) were collected retrospectively by trained abstractors from hospital records of random or consecutive samples of patients admitted to participating hospitals (three tertiary; 18 non-tertiary) with a primary discharge diagnosis of ACS, as verified by application of a pre-specified case definition: clinical diagnosis of ACS stated in the case record and either elevated cardiac troponin level or electrocardiographic changes of acute ischaemia.[7] For each therapy, only eligible patients with no contraindications were subject to analysis. Sample size at each site was determined by the availability of local resources for abstraction and total numbers of patients admitted with ACS.

The methods were approved by the Medical Quality Program Management Committee, a gazetted quality assurance committee of Queensland Health. Patient data were de-identified for analysis and are reported as aggregate data.

Risk prediction rules

In predicting risk, we sought rules derived from prospective contemporary datasets, preferably validated in unselected patients with ACS, which scored risk as a continuous variable based on readily identifiable clinical characteristics (Box 1).

TRI score

The Thrombolysis In Myocardial Infarction (TIMI) Risk Index (TRI) is a registry-validated tool for predicting in-hospital mortality in both STEMI and NSTEMI based on age, heart rate and blood pressure measured on presentation.[15,16] This tool grouped patients with STEMI or NSTEMI as low risk (in-hospital mortality < 10%

1 Risk scores

Risk score	TRI[15,16]	TIMI[17]	FRISC[18]	GRACE[19]
Predicted outcome	In-hospital all-cause death in patients with STEMI or NSTEMI	14-day risk of all-cause death, new or recurrent MI, or severe ischaemia requiring urgent revascularisation in patients with NSTEMI/UA	6-month risk of all-cause death or recurrent MI in patients with NSTEMI/UA	6-month risk of all-cause death in ACS patients surviving to discharge
Scoring method	(Heart rate × age/10)^2/SBP (mmHg)	Score 1 point for each factor and add: • Age > 65 years • 3 risk factors (diabetes, smoker, hypertension, hyperlipidaemia, FH) • Past coronary event • ST deviation on presentation ECG • At least 2 anginal events in the past 7 days • Positive troponin • Acetylsalicylic acid use in the past 7 days	Score 1 point for each risk factor and add: • Age ≥ 70 years • Male sex • Diabetes • Previous acute MI • ST depression on presentation ECG • Positive troponin	Score according to variable and add: • Age (years): ≤ 39, 0; 40–49, 18; 50–59, 36; 60–69, 55; 70–79, 73; 80–89, 91; ≥ 90, 100 • History of CHF, 24 • History of acute MI, 12 • Heart rate (beats/min): < 50, 0; 50–69, 3; 70–89, 9; 90–109, 14; 110–149, 23; 150–199, 35; ≥ 200, 43 • SBP (mmHg): < 80, 24; 80–99, 22; 100–119, 18; 120–139, 14; 140–159, 10; 160–199, 4; ≥ 200, 0 • ST depression, 11 • Serum creatinine (mg/dL): 0–0.39, 1; 0.4–0.79, 3; 0.8–1.19, 5; 1.2–1.59, 7; 1.6–1.99, 9; 2–3.99, 15; ≥ 4, 20 • Elevated cardiac enzymes, 15 • No in-hospital PCI, 14
Risk score categories and predicted event rates	*Risk score* / *Event rate (STEMI/NSTEMI)* Low < 30 / < 10%/< 7% Mod 30–60 / 10%–30%/7%–20% High > 60 / > 30%/> 20%	*Risk score* / *Event rate* Low 0–2 / ≤ 8% Mod 3–4 / 13%–20% High 5–7 / 26%–40%	*Risk score* / *Event rate* Low 0–2 / 5%–9% Mod 3–4 / 13%–20% High 5–6 / 37%	*Risk score* / *Event rate* Low < 120 / < 5% Moderate 120–145 / 5%–10% High > 145 / > 10%
Test/validation c statistics	STEMI: 0.79/0.85 NSTEMI: 0.73/0.75	0.65/0.63	0.70/(no validation)	0.81/0.75
Treatment application	Reperfusion therapy in STEMI Heparin in STEMI/NSTEMI	Early coronary angiography in NSTEMI/UA	Early coronary angiography in NSTEMI/UA	Adjuvant treatments prescribed at discharge in all ACS patients surviving to discharge

ACS = acute coronary syndrome. CHF = congestive heart failure. ECG = electrocardiogram. FH = family history of premature coronary heart disease. FRISC = Fragmin and fast Revascularization during InStability in Coronary artery disease. GRACE = Global Registry of Acute Coronary Events. MI = myocardial infarction. NSTEMI = non-ST-elevation myocardial infarction. PCI = percutaneous coronary intervention. SBP = systolic blood pressure. STEMI = ST-elevation myocardial infarction. TIMI = Thrombolysis In Myocardial Infarction. TRI = TIMI Risk Index. UA = unstable angina. ◆

and < 7%, respectively), moderate risk (10%–30% and 7%–20%) and high risk (> 30% and > 20%), based on computed scores of < 30, 30–60 and > 60, respectively. We used the TRI score to relate risk level to the frequency with which eligible patients with STEMI received reperfusion therapy and those with STEMI and NSTEMI received heparin within the first 24 hours of presentation.

TIMI score

The TIMI score was derived as a tool for prioritising use of an early (within 48 hours of presentation) invasive strategy comprising coronary angiography and, if indicated, PCI in patients with NSTEMI/UA.[17] The score, calculated on admission, predicts risk of death, new or recurrent MI or ischaemia requiring urgent revascularisation at 14 days, and categorises patients as low risk (score, 0–2; event rate, ≤ 8%), moderate risk (score, 3–4; event rate, 13%–20%) or high risk (score, 5–7; event rate, 26%–40%).

FRISC score

For patients with NSTEMI/UA, the Fragmin and fast Revascularization during InStability in Coronary artery disease (FRISC-II) trial investigators developed a score, measured at presentation, to stratify risk of death or AMI at 6 months in relation to the use of an early invasive strategy: low risk (score, 0–2; event risk, 5%–9%), moderate risk (score, 3–4; event risk, 13%–20%) and high risk (score, 5–6; average event risk, 37%).[18]

GRACE score

Investigators from the Global Registry of Acute Coronary Events (GRACE) derived and validated a rule, used at discharge, to predict risk of death at 6 months in patients with ACS.[19] We used this rule to categorise patients surviving to discharge and not transferred to other institutions as being low risk (score, < 120; mortality, < 5%), moderate risk (score, 120–145; mortality, 5%–10%) and high risk (score, > 145; mortality, > 10%), and related this risk to use of adjuvant therapies at discharge.

2 Variation in treatment intensity with level of risk

	Eligible patients receiving treatment								
	Low risk		Moderate risk		High risk		All patients		*P* (for linear trend)
Treatment	No	%	No	%	No	%	No	%	
Reperfusion therapy	476/539	88.3%	91/147	61.9%	2/11	18.2%	569/697	81.6%	< 0.001
Heparin	1911/2091	91.4%	744/889	83.7%	110/151	72.8%	2765/3131	88.3%	< 0.001
Early coronary angiography									
TIMI score	139/414	33.6%	149/621	24.0%	24/130	18.5%	312/1165	26.8%	< 0.001
FRISC score	119/607	19.6%	258/1575	16.4%	33/288	11.5%	410/2470	16.6%	0.002
Antiplatelet agents	1027/1051	97.7%	618/637	97.0%	515/537	95.9%	2160/2225	97.1%	0.063
β-Blockers	631/725	87.0%	368/416	88.5%	322/407	79.1%	1321/1548	85.3%	< 0.001
ACE inhibitors/ angiotensin receptor antagonists	128/155	82.6%	129/150	86.0%	207/263	78.7%	464/568	81.7%	0.088
Lipid-lowering agents	805/922	87.3%	442/521	84.8%	294/447	65.8%	1541/1890	81.5%	< 0.001
Referral for OCR	505/974	51.8%	250/544	46.0%	137/398	34.4%	892/1916	46.6%	< 0.001
In-hospital mortality*	23/2605	0.9%	47/1101	4.3%	19/169	11.2%	89/3875	2.3%	< 0.001

ACE = angiotensin-converting enzyme. FRISC = Fragmin and fast Revascularization during InStability in Coronary artery disease. OCR = outpatient cardiac rehabilitation. TIMI = Thrombolysis In Myocardial Infarction. * Risk-specific mortality rates according to TIMI Risk Index (TRI) categorisation; data required to calculate TRI score were missing for 37 of 3912 patients. ◆

Statistical analysis

Differences between risk categories in the proportions of eligible patients receiving specific treatments were assessed using χ^2 measures of trend or of association, as appropriate. Differences in prevalence of clinical characteristics among eligible patients who did or did not receive specific treatments were assessed using 2 × 2 contingency tables. Independent predictors of treatment use were identified by multivariable logistic regression models, with effect size expressed as odds ratio (OR) with 95% confidence interval. Predictor variables were entered into the model if associated with $P < 0.10$ on univariate analysis, with independent predictors chosen by forward selection.

RESULTS

During the study period, 3912 patients met our case definition and had evaluable data. Their mean (SD) age was 65.4 (14.1) years, 67% were men, 88% had troponin-positive ACS (STEMI, 28%; NSTEMI, 60%), and 72% presented directly to emergency departments of non-tertiary hospitals. Just over a third had prior history of ACS (39%), and more than a quarter had one or more risk factors of hypertension (51%), hyperlipidaemia (41%), diabetes (25%), and current smoking status (28%).

Differences between risk categories in frequency of treatment use are listed in Box 2.

Early reperfusion

Applying the TRI score to 697 eligible patients, a significant inverse relation was seen between risk level and the proportion of patients receiving reperfusion therapies (low risk, 88.3%; moderate risk, 61.9%; high risk, 18.2%; *P* for trend < 0.001).

Use of heparin

Applying the TRI score to 3131 eligible patients, significantly more low- and moderate-risk patients received heparin than did high-risk patients (low risk, 91.4%; moderate risk, 83.7%; high risk, 72.8%; *P* for trend < 0.001).

Early invasive intervention

Applying the TIMI score to 1165 eligible patients, significantly more low- and moderate-risk patients received early invasive intervention than did high-risk patients (33.6%, 24.0%, and 18.5%, respectively; *P* for trend < 0.001). Applying the FRISC score to 2470 eligible patients revealed the same pattern: 19.6%, 16.4%, and 11.5%, respectively; *P* for trend = 0.002).

Adjuvant therapies at discharge

Based on the GRACE score, there were no significant differences between low-, moderate- and high-risk categories in the use of antiplatelet agents among 2225 eligible patients (97.7%, 97.0%, and 95.9%, respectively) or use of angiotensin-converting enzyme inhibitors and angiotensin II receptor antagonists among 2950 eligible patients (82.6%, 86.0%, and 78.7%, respectively). Significantly more low- and moderate-risk than high-risk eligible patients received β-blockers (87.0%, 88.5%, and 79.1%, respectively; *P* for trend < 0.001), lipid-lowering agents (87.3%, 84.8%, and 65.8%, respectively; *P* for trend < 0.001) and referral to cardiac rehabilitation (51.8%, 46.0%, and 34.4%, respectively; *P* for trend < 0.001).

Predictors of therapy use

Independent predictors of use of specific therapies are listed in Box 3. A coded principal discharge diagnosis of AMI was significantly associated with increased use of reperfusion therapies (OR, 19.67), heparin (OR, 2.25), β-blockers (OR, 1.77), lipid-lowering agents (OR, 2.15) and referral for cardiac rehabilitation (OR, 1.46). A lower use of reperfusion therapies was significantly associated with past hypertension (OR, 0.60), previous cerebrovascular accident (CVA) (OR, 0.10), past atrial tachyarrhythmias (OR, 0.11), diabetes (OR, 0.53), and older age (OR, 0.36). A greater use of heparin was predicted by angiography performed during admission (OR, 1.94), whereas older age (OR, 0.70), heart failure (OR, 0.53) or atrial tachyarrhythmias (OR, 0.55) predicted a lower use. Early coronary angiography was more likely to occur in patients admitted to tertiary hospitals (OR, 2.80) and less likely in those with past hypertension (OR, 0.76) or past ACS (OR, 0.62–0.73).

Use of antiplatelet agents was more prevalent in patients who underwent angiography (OR, 3.47) or had known hyperlipidaemia (OR, 2.21) and less prevalent in those with past atrial tachyarrhythmias (OR, 0.43). β-Blockers were used more often in patients with systolic blood pressure ⩾ 180 mmHg on admission (OR, 1.81) or positive troponin (OR, 1.60) and less often in those with past heart failure (OR, 0.55) or CVA (OR, 0.51), low systolic blood pressure

3 Independent predictors of treatment use*

Variable	Odds ratio	95% CI
Reperfusion		
AMI as principal discharge diagnosis	19.67	7.59–50.97
ST segment deviation	2.29	1.29–4.09
Male sex	1.76	1.05–2.97
Past history of hypertension	0.60	0.37–0.98
Diabetes	0.53	0.31–0.92
Past history of acute coronary syndrome	0.52	0.32–0.85
Age ⩾ 70 years	0.36	0.22–0.59
Past history of atrial tachyarrhythmias†	0.11	0.03–0.45
Past history of cerebrovascular accident	0.10	0.02–0.51
Heparin		
AMI as principal discharge diagnosis	2.25	1.76–2.89
Angiography performed during admission	1.94	1.49–2.53
Past history of hypertension	1.54	1.13–2.10
Hyperlipidaemia	1.30	1.03–1.64
Risk factors‡	0.81	0.67–0.99
Age ⩾ 70 years	0.70	0.55–0.89
Past history of atrial tachyarrhythmias†	0.55	0.37–0.80
Past history of congestive heart failure	0.53	0.38–0.74
Early coronary angiography		
TIMI score		
Admission to tertiary hospital	2.80	1.95–4.05
Diabetes	0.62	0.42–0.92
Past history of acute coronary syndrome	0.62	0.42–0.90
FRISC score		
Admission to tertiary hospital	2.04	1.51–2.75
Hypertension	0.76	0.58–0.99
Past history of acute coronary syndrome	0.73	0.55–0.97
Antiplatelet agents		
Angiography performed during admission	3.47	1.25–9.63
Hyperlipidaemia	2.21	1.25–3.92
Past history of atrial tachyarrhythmias†	0.43	0.19–0.98
β-Blockers		
High systolic BP (⩾ 180 mmHg) on admission	1.81	1.06–3.08
AMI as principal discharge diagnosis	1.77	1.24–2.52
Positive troponin	1.60	1.03–2.46
ST segment deviation	1.33	1.01–1.74
Risk factors‡	1.28	1.06–1.54
Angiography performed during admission	0.67	0.46–0.98
Age ⩾ 70 years	0.63	0.47–0.85
Current smoker	0.56	0.37–0.83
Past history of congestive heart failure	0.55	0.35–0.85
Past history of cerebrovascular accident	0.51	0.28–0.92
Low systolic BP (⩽ 90 mmHg) on admission	0.45	0.20–1.00
Angiotensin-converting enzyme inhibitors/angiotensin receptor II antagonists		
Hyperlipidaemia	1.94	1.23–3.08
Male sex	1.85	1.20–2.84
Lipid-lowering agents		
Hyperlipidaemia	4.69	3.43–6.40
Past history of coronary artery bypass grafting	2.28	1.33–3.91
AMI as principal discharge diagnosis	2.15	1.63–2.83
Angiography performed during admission	1.73	1.15–2.63
Male sex	1.44	1.11–1.88
Past history of acute coronary syndrome	0.61	0.46–0.80
Past history of congestive heart failure	0.58	0.39–0.87
Past history of atrial tachyarrhythmias†	0.58	0.36–0.68
Age ⩾ 70 years	0.52	0.39–0.68
Referral for outpatient cardiac rehabilitation		
Angiography performed during admission	3.21	2.16–4.77
Positive troponin	2.01	1.43–2.83
AMI as principal discharge diagnosis	1.46	1.13–1.89
ST deviation	1.21	1.02–1.43
Risk factors‡	1.10	1.01–1.21
High systolic BP (⩾ 180 mmHg) on admission	0.68	0.50–0.93
Past history of acute coronary syndrome	0.66	0.54–0.81
Age ⩾ 70 years	0.64	0.52–0.78
Admission to tertiary hospital	0.61	0.42–0.89
Past history of cerebrovascular accident	0.49	0.25–0.95

*Candidate predictors entered into the model for every indicator comprised past history of acute coronary syndrome, congestive heart failure, cerebrovascular accident or atrial tachyarrhythmias; documented presence of diabetes, hypertension, hyperlipidaemia, peripheral vascular disease, severe chronic obstructive pulmonary disease ("end-stage" or "steroid or oxygen-dependent"), or renal insufficiency (serum creatinine > 150 μmol/L); sex; age; smoking status; multiple risk factors‡; ST deviation on admission electrocardiogram; positive or negative troponin level measured within 12 hours of admission; blood pressure and heart rate documented at presentation; type of admitting hospital (tertiary v non-tertiary); AMI as principal discharge diagnosis; and angiography performed during admission. † Atrial tachyarrhythmias defined as chronic or paroxysmal atrial fibrillation or flutter. ‡ Risk factors defined as three or more of hypertension, hyperlipidaemia, diabetes, smoker, family history of premature cardiovascular disease. AMI = acute myocardial infarction. BP = blood presure. FRISC = Fragmin and fast Revascularization during InStability in Coronary artery disease. TIMI = Thrombolysis In Myocardial Infarction. ◆

(⩽ 90 mmHg) on admission (OR, 0.45), or who were current smokers (OR, 0.56). Lipid-lowering agents were more frequently used in male patients (OR, 1.44) and those with known hyperlipidaemia (OR, 4.69), previous coronary artery bypass grafting (OR, 2.28) or coronary angiography (OR, 1.73), and less frequently in those with past atrial tachyarrhythmias (OR, 0.58), heart failure (OR, 0.58) or ACS (OR, 0.61), or who were of older age (OR, 0.52). Referral for cardiac rehabilitation was more likely if angiography occurred during admission (OR, 3.21), troponin was positive (OR, 2.01) or patients had multiple risk factors (OR, 1.10) but less likely in the presence of older age (OR, 0.64), previous CVA (OR, 0.49) or ACS (OR, 0.66), or admission to a tertiary hospital (OR, 0.61).

Factors most frequently associated with greater treatment use were angiography per-

formed during admission and a coded principal discharge diagnosis of AMI (4 of 8 treatments), and known hyperlipidaemia (3 of 8). Factors most frequently associated with less treatment use were older age (5 of 8), past ACS or atrial tachyarrhythmias (4 of 8), and past CVA or heart failure (3 of 8).

DISCUSSION

Our study of unselected patients with ACS admitted to multiple hospitals revealed that for most (6 out of 8) evidence-based therapies, frequency of use was significantly lower in high-risk than in lower-risk patients after accounting for therapy contraindications at the level of the individual patient. Risk–treatment discordance was greatest for reperfusion therapies, early invasive intervention, lipid-lowering drugs and referral to cardiac rehabilitation. Older age and past history of atrial tachyarrhythmias, ACS, CVA, and heart failure were associated with a lower propensity to use multiple treatments.

Comparisons with other studies

Three other studies similar to ours in design have shown an inverse relationship between risk and intensity of one or more treatments.[20-22] In a large United States study of 77 760 patients with non-ST-elevation ACS, predictors of increased treatment intensity comprised care provided by cardiologists, ST segment deviation on electrocardiography and positive cardiac markers, while predictors of decreased use included signs of heart failure, renal insufficiency and advanced age.[20] In a smaller Canadian study of similar patients ($n = 4414$), cardiologist care and on-site cardiac catheterisation predicted increased use of in-hospital cardiac catheterisation.[21] In the third study of 2829 patients with STEMI, the use of reperfusion therapy fell 4% with every 1% increase in baseline risk, and fell 18% with each additional pre-existing chronic comorbidity.[22]

Other studies have confirmed older age to be a frequent predictor of treatment omission,[9,10] and an association between lower treatment intensity, particularly for reperfusion therapies and early coronary angiography, and atrial tachyarrhythmias,[23] heart failure[24] and diabetes.[11] The strong positive association seen here between tertiary hospital admission and early coronary angiography has been confirmed in other studies;[25,26] for all other treatments in our study, risk–treatment mismatch was no different between tertiary and non-tertiary hospitals. The association between undergoing angiography and receiving antiplatelet agents and lipid-lowering agents has been noted elsewhere,[27] as have associations between sex and reperfusion therapies, afterload-reducing drugs and lipid-lowering agents.[28] Contrary to some studies,[12,20] we did not find the presence of renal insufficiency to be predictive of lower treatment intensity. Finally, a past history of ACS appeared to predict a more conservative approach independently of age and other comorbidities, which has not been previously reported.

Correlation between treatment omission and outcomes

Knowing which treatment omissions in eligible patients with ACS account for most of the avoidable mortality and morbidity would assist in targeting quality improvement strategies. Unfortunately, different studies report conflicting findings. In one study, omission of timely reperfusion at presentation and of aspirin and β-blockers at discharge accounted for most of the variance in 30-day risk-standardised mortality rates for AMI between 899 hospitals.[29] Another study found omission of glycoprotein IIb/IIIa inhibitors shortly after admission and of clopidogrel and lipid-lowering agents at discharge correlated most strongly with higher risk-adjusted in-hospital mortality rates among patients with NSTEMI/UA admitted to 350 hospitals.[30] Finally, in another study, omission of an invasive strategy in patients with AMI was the only significant predictor of sudden cardiac death at 3 years.[31] Until more consistent analyses become available, quality improvement programs are obliged to focus on all effective treatments.

Study limitations

Our sampling rate of admissions to all participating hospitals with AMI as the principal discharge diagnosis was about 8% (3490/42 140), which limits generalisability of our findings. We may not have captured all patient characteristics (medical comorbidities, psychosocial factors) that might justifiably incline clinicians towards withholding specific therapies in individual patients, especially very elderly patients and others at high risk. In-hospital mortality observed in our study was considerably less than that predicted by the TRI score, which we postulate is due to a lower disease severity and comorbidity prevalence in our cohort compared with the two cohorts (STEMI[15] and NSTEMI[16]) used in deriving the TRI: diabetes, 25% v 26%–33%; past heart failure, 7.9% v 13.8%–24%; past CVA, 3.6% v 9.1%–12.9%; and previous coronary revascularisation, 12.8% v 19.9%–28.1%. A validated score derived from the GRACE data for assessing in-hospital mortality could not be used, despite better performance characteristics than the TRI (*c* statistic 0.84 v 0.73–0.79),[32] because one requisite variable (Killip class) was not collected in our dataset. Also, the FRISC risk score[18] has not been validated in unselected ACS populations, but directly estimated benefit of an invasive strategy in patients with NSTEMI/UA within a large randomised trial. The number of high-risk patients for the reperfusion indicator was small ($n = 11$), and patients to which the TIMI score was applied were substantially fewer in number than for the FRISC score, as measurement of all TIMI variables did not commence until mid 2004.

Implications for practice improvement

Clinicians may withhold evidence-based therapies from higher-risk patients for several reasons. First, whether the benefits or minimal harm seen in trial patients apply to patient groups who were excluded may be uncertain. In the case of reperfusion therapies or invasive strategies, our results suggest that many clinicians view older age (≥ 70 years) and past history of hypertension or CVA as potential risk factors for bleeding. In contrast, GRACE data suggest advanced age (>85 years), female sex, history of bleeding and renal insufficiency independently predict higher bleeding risk.[33]

Second, while risk of harm may be overestimated, the magnitude of treatment-related benefit in high-risk populations may be underestimated. For example, in one trial, routine early invasive management versus medical therapy in non-ST-segment elevation ACS conferred an overall absolute risk reduction (ARR) in death and AMI at 6 months of 4.8 percentage points (8.8% v 13.6%; $P = 0.02$), but in patients older than 75 years, ARR was 10.8 percentage points (10.8% v 21.6%; $P = 0.02$).[34] Greater use of simple, standardised, bedside tools for calculating patient risk at presentation or discharge (such as those described here), coupled with estimates, within guidelines, of treatment-induced ARR for specific patient subgroups may facilitate more accurate estimates of baseline risk and benefit and assist in prioritising access to treatment.

Third, the cost-effectiveness of aggressively treating particular patient groups, especially older patients, may be an issue, although, in the case of lipid-lowering agents, economic evaluations suggest reasonable returns on investment.[35]

Finally, the two- to threefold greater use of angiography in eligible patients admitted to tertiary than to non-tertiary hospitals indicates inequity in access to invasive management. This lends support to implementing regionalised networks of tertiary and non-tertiary institutions which assign angiography slots based on need (using standardised, risk-based referral and transfer procedures[36,37]) and which aim to increase overall angiography rates during index admission from the current average of 27% of eligible patients.

CONCLUSION

In routine care of patients with ACS, eligible patients at high risk receive treatment less frequently than low-risk patients. Targeted professional education, risk stratification tools, guideline recommendations linked with population-specific estimates of ARR, and hospital networking and risk-based referral procedures for invasive services may all help to better align treatment with risk.

ACKNOWLEDGEMENTS

The members of the CPIC Cardiac Collaborative in addition to the authors are: Bundaberg Hospital: Dr Andre Conradie, Vivienne Tapiolas; Caboolture/Redcliffe Hospitals: Dr Robin Bradbear, Dr Peter Stride, Kylie Hillier; Cairns Hospital: Dr Prasad Challa, Yvonne Hodder, Karyn Greensill, Donna Kreuter; Gladstone Hospital: Dr Peter Durman, Julie McRae, Jacqui Bulbrook; Gold Coast Hospital: Dr Nick Buckmaster, Dr Greg Aroney, Vicky Syme; Hervey Bay Hospital: Marilyn Jensen; Ingham Hospital: Janine Johnson, Judy Cardillo; Innisfail Hospital: Majella van Tienan, Dr Peter McKenna; Ipswich Hospital: Dr Jane Hoare, Dr Mandeep Mathur, James Mitchell; Logan Hospital: Dr Jeffrey Franco, Katrina Chisholm; Maryborough Hospital: Dr Alan Jones, Kylie Lenthall; Mackay Hospital: Dr Belinda Weich, Lyn Gralow; Nambour Hospital: Dr Steven Coverdale, Megan Courtney; Princess Alexandra Hospital: Dr Paul Garrahy, Melodie Downey, Michelle Winning; Queen Elizabeth II Hospital: Dr Judy Flores; Royal Brisbane and Women's Hospital: Dr John Atherton, Damien Otago; Redland Hospital: Dr David Henderson, Karen Pratt; Rockhampton Hospital: Dr Raj Shetty, Cara Edwards; Toowoomba Hospital: Dr Spencer Toombes, Caroline Leopold, Caroline Byrne; Townsville Hospital: Dr Raibhan Yadav, Leonie Jones.

COMPETING INTERESTS

None identified.

AUTHOR DETAILS

Ian A Scott, FRACP, MHA, MEd, Director of Internal Medicine[1] and Associate Professor[2]
Patrick H Derhy, BSc, Principal Project Officer, Clinical Practice Improvement Centre[3]
Di O'Kane, BSc, MSc, Principal Project Officer, Clinical Practice Improvement Centre[3]
Kylie A Lindsay, BN, GCICN, GCMan, Principal Project Officer, Clinical Practice Improvement Centre[3]
John J Atherton, MB BS, FRACP, PhD, Associate Professor of Medicine[2] and Director of Cardiology[3]
Mark A Jones, BSc, Biostatistician, Clinical Services Evaluation Unit[1]

1 Princess Alexandra Hospital, Brisbane, QLD.
2 University of Queensland, Brisbane, QLD.
3 Royal Brisbane and Women's Hospital, Brisbane, QLD.

Correspondence: ian_scott@health.qld.gov.au

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(Received 25 Dec 2006, accepted 24 Apr 2007) ❑