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A REPORT BY THE DIVISION OF CARDIOLOGY
ST. MICHAEL'S HOSPITAL, UNIVERSITY OF TORONTO, ONTARIO

Scientific Update™

Quality Improvement in the Management of Acute Coronary Syndromes

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A Report on Presentations at an official Satellite Symposium at the American Heart Association Scientific Sessions 2004

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Reported and discussed by:
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Randomized clinical trials have demonstrated that new pharmacologic therapy, as well as more rapid and improved revascularization techniques, can improve outcomes in patients presenting with acute coronary syndromes (ACS). While the results of these important trials have led to appropriate changes in consensus guideline recommendations, their implementation into routine clinical practice has lagged behind. Thus, a marked "care gap" exists, whereby the lack of guideline adherence has been shown to adversely affect patient outcome. This issue of *Cardiology Scientific Update* discusses recent advances in ACS care, the consensus guideline processes, and the evolution of the development of practice guidelines and strategies to achieve quality care of ACS patients in order to improve outcomes.

Recent advances and future therapies in ACS

Advances in antithrombotic and antiplatelet therapy, as well as early revascularization, have resulted in improved clinical outcomes in patients presenting with ACS.[1,2] Ongoing research in this important field continues at a rapid pace, as better and safer therapies are sought to further improve outcomes.

The PROTECT (Randomized Trial to Evaluate the Relative PROTECTion against Post-PCI Microvascular Dysfunction and Post-PCI Ischemia among Anti-Platelet and Anti-Thrombotic Agents)-TIMI 30 trial randomized 857 high-risk ACS patients undergoing early percutaneous coronary intervention (PCI) to receive either the glycoprotein (GP) IIb/IIIa inhibitor, eptifibatide, or the direct thrombin inhibitor, bivalirudin. Patients in the eptifibatide arm were further randomized to receive enoxaparin or unfractionated heparin (UFH). Results presented at the American Heart Association Scientific Sessions 2004 revealed no significant differences in the primary efficacy endpoint of coronary flow reserve post-PCI between the eptifibatide and bivalirudin-treated groups as determined by thrombolysis in myocardial infarction (TIMI) frame count, before and after adenosine, (1.33 vs 1.43, p=0.13 for all patients). The percentage of patients with TIMI myocardial perfusion grade 3 post-PCI was higher for those treated with eptifibatide compared to those treated with bivalirudin (57.9% vs 50.9%, odds ratio 1.44, 95% confidence interval (CI), 1.003-2.06, p=0.048). However, there were no significant differences in the secondary clinical endpoints of combined death/MI or death/MI/ischemia on Holter monitoring (Figure 1).

The ongoing ACUITY (Acute Catheterization and Urgent Intervention Thrombotic strategY) trial will compare bivalirudin to enoxaparin, with or without upstream GP IIb/IIIa

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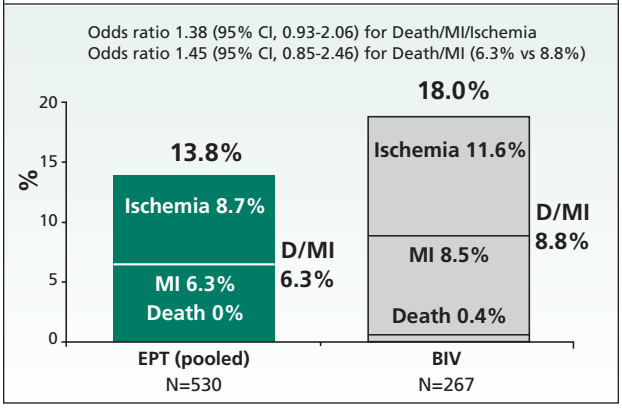
Figure 1: PROTECT – death, MI or ischemia on Holter monitoring through 48 hours



EPT = eptifibatide
BIV = bivalirudin

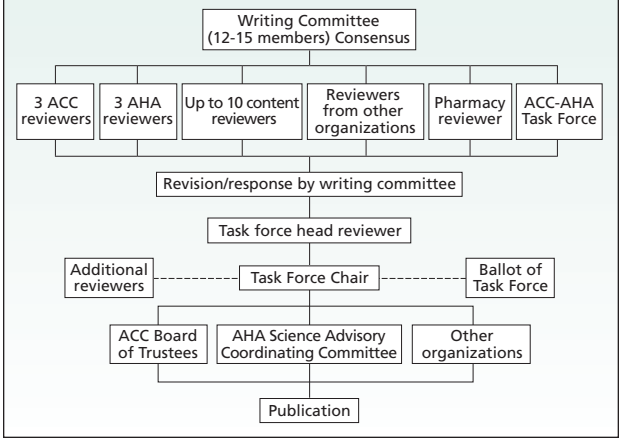
inhibitor, and plans to enroll approximately 13,800 ACS patients undergoing early invasive management to multiple treatment arms. The EARLY ACS (EARLY glycoprotein IIb/IIIa inhibition in patients with non-ST-segment elevation Acute Coronary Syndrome) plans to randomize 10,500 ACS patients to early front-loaded eptifibatide or placebo, with all patients receiving aspirin, clopidogrel, and heparin and undergoing early catheterization. Results are expected in 2006. These 2 large trials will further define the role of direct thrombin inhibitors and GP IIb/IIIa inhibitors in the acute management of ACS patients.

Newer anti-thrombotic and anti-platelet agents being studied in ACS patients include fondaparinux, a synthetic pentasaccharide that selectively inhibits activated clotting factor X, and prasugrel, a novel adenosine diphosphate antagonist. The PENTUA (Pentasaccharide in Unstable Angina) trial, a dose-finding study in ACS patients, revealed no dose response for different fondaparinux doses, along with similar efficacy and safety for fondaparinux versus enoxaparin.[3]

Two large trials will evaluate the benefits of fondaparinux compared to heparin in ACS patients: the OASIS (Organization to Assess Strategies for Ischemic Syndromes)-5 and 6 trials. In total, these 2 studies will evaluate 26,000 patients in different ACS populations, with OASIS-5 enrolling non ST-segment elevation MI and OASIS-6 enrolling acute ST-segment elevation MI patients.

The JUMBO (Joint Utilization of Medications to Block platelets Optimally) TIMI-26 trial was recently presented at the European Society of Cardiology Congress 2004. This phase 2, double-blind, dose-finding study randomized 904 patients undergoing either elective or urgent PCI to 2 different loading doses of prasugrel and 3 different maintenance dosages, or standard clopidogrel treatment. At 30-day follow-up, there were no significant differences between prasugrel and clopidogrel with regard to the primary endpoint of significant non-coronary artery bypass graft (CABG) bleeding at 30 days, regardless of the administered prasugrel dose. The secondary clinical endpoint was a composite of major adverse cardiac events (MACE), defined as death, target vessel revascularization, or documented total occlusion, MI, stroke, and recurrent ischemia through 30 days. MACE rates were similar among the groups (7.2% vs 9.4%, p=0.31). There was a trend toward a lower MI rate (5.7% vs 7.9%, p=0.21) and lower rate of recurrent ischemia (1.7% vs 3.5%, p=0.09) in the prasugrel arm.

Figure 2: Flow diagram of the ACC/AHA review process



The planned MICHELANGELO TIMI-38 trial will enroll 13,000 ACS patients undergoing PCI to receive either prasugrel or clopidogrel, and should help further define the role of this new anti-platelet agent in ACS management.

Cardiology Practice Guidelines

In the present era, when clinical trials are performed and published at a rapid rate, incorporating these latest results into routine practice has become exceedingly difficult for the busy clinician. Thus, the role of specific practice guidelines has become increasingly more important. The American College of Cardiology (ACC)/American Heart Association (AHA) practice guidelines[4,5] are consensus documents formed on the basis of evidence-based medicine, along with expert opinion (Figure 2). The rationale for the very first ACC/AHA guidelines on permanent pacemaker implantation[6] in 1984 was to detail the appropriate indications for pacemakers and ensure adequate justification for their implantation. Over the years, the guidelines have evolved from focusing primarily on procedures (eg, electrocardiography [ECG] or coronary angiography), to a more disease-based approach,

Table 1: Classification of recommendations and level of evidence utilized in ACC/AHA clinical practice guidelines

Classification of recommendations	
Class I	Intervention is useful and effective
Class IIa	Weight of evidence/opinion is in favour of usefulness/efficacy
Class IIb	Usefulness/efficacy is less well established by evidence/opinion
Class III	Intervention is not useful/effective and may be harmful
Level of evidence	
Level A	Data from many large RCTs
Level B	Data from fewer, smaller RCTs, careful analyses of nonrandomized studies and observational registries
Level C	Expert consensus

RCT = randomized controlled trial

such as unstable angina and non-ST-elevation MI, to help practicing physicians with clinical decision-making in patient management and provide the underpinnings for quality improvement activities.

Input into these guidelines comes from multiple relevant professional organizations, (eg, European Society of Cardiology and the Canadian Cardiovascular Society), encompassing pharmacists, cardiologists and cardiovascular surgeons, and involving an extensive and rigorous review process. Standardized classifications were adopted by the ACC/AHA Task Force several years ago to ensure consistency. The recommendations provided within the guidelines are categorized into classes of recommendations[4] (Class I, IIa, IIb, and III), and levels of evidence (A, B, and C) (Table 1). Since their inception, the quality of the evidence on which the recommendations are based has steadily improved. In the early guidelines (1984-1990), approximately one-third of the recommendations were Class I, while in the most recent guidelines for management of ST-elevation MI,[7] 58% are Class I. However, many of these Class I recommendations were made without the strongest weight of evidence, with only 14.1% at the level of evidence A. This emphasizes the need for ongoing clinical research, along with the rapid integration of results into practice guidelines, to strengthen the guidelines and further improve patient care.

To keep up with rapid advances in cardiovascular care, the ACC/AHA adopted a policy to shorten the time period required to update and revise existing practice guidelines, allowing the committees to incorporate new evidence and put it into clinical practice in a timely fashion. Thus, the practice guidelines would act as a "living" document, constantly evolving and changing as new evidence arises. The obvious benefits would be the rapid incorporation of new evidence reflecting up-to-date science and the opportunity to make topic changes across multiple guidelines at one time. The potential downsides are the extensive time, effort, and commitment, as well as the significant costs needed to implement and maintain the guidelines in a current perspective. In addition, the rapid pace of change would mean that performance measures would also be constantly changing, rendering these quality care measures less feasible and more difficult to implement. Overall, these guidelines have evolved to reflect the highest ideals of medicine and represent a strong sustained commitment to improvement in the quality of cardiovascular care worldwide.

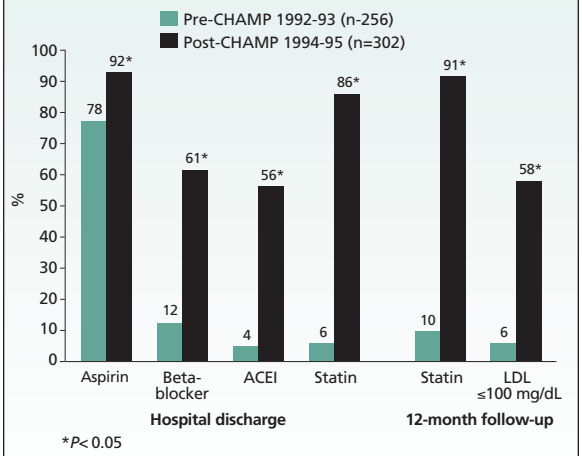
Quality improvement in ACS

Over the past decades, important research has led to remarkable progress in cardiovascular care. At the same time, the ACC and AHA, along with other organizations worldwide, have translated these important clinical trial findings into updated clinical practice guidelines. It was assumed that recommendations would be seamlessly applied to clinical practice, leading to direct patient benefit. Unfortunately, recent studies have shown that therapies recommended in practice guidelines are not applied as consistently as desired and that a marked "care gap" exists between guideline recommendations and patient care. Furthermore, registries have demonstrated a direct link between patient outcome and guideline adherence, supporting the need for specific quality improvement initiatives.

Many quality improvement programs are initiated during patient hospitalization. The advantages of such programs are two-fold. First, when ACS patients are hospitalized, patient and family attention is at its highest, resulting in more effective teaching of evidence-based care and improved long-term adherence to therapy.[8] Secondly, the hospital environment provides the necessary infrastructure for standardized processes, protocols, and teams to function and allows for continuous process evaluation and improvements.

The Cardiac Hospital Atherosclerosis Management Program (CHAMP) was a single-centre, hospital-based, quality improvement program targeting patients hospitalized with established coronary artery disease (CAD).[9] It focused on the initiation of medications proven beneficial for secondary pre-

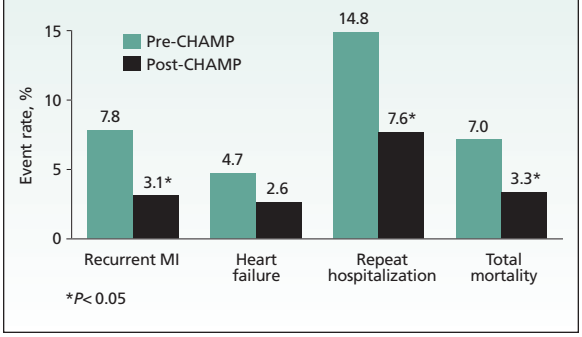
Figure 3: Treatment rates in CAD patients before and after CHAMP quality improvement implementation.



vention, namely aspirin, hydroxymethylglutaryl coenzyme A (HMG-CoA)-reductase inhibitors (statins), beta-blockers, and angiotensin-converting enzyme inhibitors (ACEIs), prior to hospital discharge. Treatment rates and clinical outcomes were compared in patients for the 2-year period prior to, and after, the 2-year period of CHAMP implementation. Treatment rates with all 4 medications increased significantly in the post-CHAMP era, with more patients achieving low-density lipoprotein (LDL) cholesterol target levels (Figure 3). This improved adherence to practice guidelines resulted in dramatically improved clinical outcomes in patients post-CHAMP (Figure 4).

The AHA and ACC have separately developed large-scale hospital-based programs in an effort to implement

Figure 4: Clinical outcomes in CAD patients before and after CHAMP quality improvement implementation.



guidelines and improve the overall quality of patient care, specifically the ACS population. The Get With the Guidelines (GWTG) program is a hospital-based quality improvement initiative created by the AHA and the American Stroke Association to improve the care of patients with CAD and stroke.[10] The current GWTG database has enrolled just under 157,000 CAD patients in 473 participating hospitals, using a web-based patient management tool to improve secondary prevention management. Data entry screens automatically remind physicians about specific treatment goals, provide feedback, and help evaluate adherence to guidelines. When completed, a letter directed to the primary care physician is generated, documenting discharge orders, thus reinforcing interventions that need to be continued in the outpatient setting. The application of guideline recommendations occurs at the point of care, with immediate feedback, rather than by retrospective analysis, resulting in continuous quality improvement. As an incentive, the AHA nationally recognizes hospitals that have an infrastructure for quality improvement in place and awards those who achieve compliance in 85% of CAD patients in 5 key areas (smoking cessation counseling, and aspirin, beta-blocker, ACEI and statin use). Data presented at the AHA Scientific Sessions 2004 demonstrated that the GWTG program increases adherence to guidelines and a steady improvement in all quality measures after 2 years.[11]

At the same time, the ACC established the Guidelines Applied to Practice (GAP) program to address the care of acute MI patients.[12] Its goals were to test tools and strategies to measure quality indicators and implement guidelines at the point of care, creating systems that would lead to improved performance. The initial GAP program involved nearly 400 cardiologists in 33 hospitals in Michigan, U.S.A. A 7-component tool-kit was implemented (Table 2).[12] After 12 months, a reduction in

Table 2: 7-component tool-kit implemented in the ACC GAP program for acute MI[12]

- Standard orders
- Pocket guidelines and pocket card
- Clinical pathway
- Patient information form
- Patient discharge form
- Hospital performance chart
- Chart stickers

Table 3: Features commonly associated with successful quality improvement initiatives

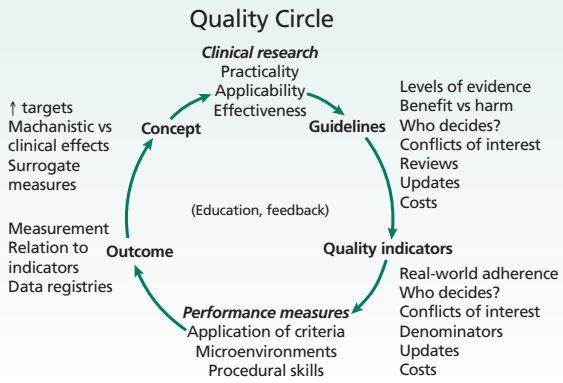
- Committed and dedicated leaders
- Standing admission and discharge orders
- Provider-specific feedback
- Appropriate infrastructure and resources
- Hospital-based program, with extension to outpatient environment
- Multidisciplinary involvement
- Regular education, dissemination and feedback
- Strive for perfection

in-hospital mortality was observed (11.9% to 9.1%), with significant improvement in the use of aspirin, beta-blockers, ACEIs, and statins. The data also demonstrated an even greater improvement in lifestyle indicators (eg, smoking cessation and dietary counseling). Given these positive results, the ACC plans to invest in other GAP initiatives for different conditions.

Another important quality improvement program is the national quality improvement initiative CRUSADE (Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA guidelines).[13] This program collects data from over 400 hospitals to analyze current treatment practices and determines the degree of guideline compliance. Results are then reported back to U.S. hospitals, informing them of individual institutional performance, along with the national rates of adherence for comparison. Thus, in contrast to the GWTG and GAP programs, feedback and evaluation in CRUSADE are reported back to institutions at a later date. Data from 47,000 high-risk ACS patients in CRUSADE has demonstrated the inverse relationship between guideline adherence and clinical outcomes.[14] In hospitals in the leading quartile for adherence to guidelines, in-hospital mortality was 3.6%, as compared to 5.9% in hospitals in the lagging quartile, thus emphasizing the importance of achieving quality improvement in patient care.

Quality improvement initiatives are ongoing in other countries, including European nations and Canada. While there exists a number of individual national registries within Europe, the CARDS (Cardiology Audit and Registration Data Standards) project aims to merge multiple registries, using common data standards for 3 modules of cardiovascular health information systems: ACS, PCI,

Figure 5: Proposed model for quality improvement cycle.



and clinical electrophysiology.[15] It would potentially result in a more efficient means of achieving quality improvement within these 3 areas in European countries.

Within Canada, several quality improvement initiatives exist. One example is the MACSTRAK (Managing the Acute Coronary Syndromes - A TRAcKing) project. Data are collected on all patients admitted to coronary care units (CCUs), cardiac wards, and emergency departments in participating hospitals and sent to a central site. Information is sent back to participating sites at regular intervals with each site using their own data to implement institutional programmatic changes and improve performance and outcomes.

Thus, multiple models exist for quality improvement worldwide. While they all have similar goals, they differ in their approach to achieving these goals. There are, however, a number of features commonly associated with improved and sustained improvements in quality care (Table 3). Ideally, quality improvement is an ongoing, continuous cycle, from scientific advancement with clinical research, to practice guideline update and revision, to determination of quality indicators and performance measures driving quality improvement initiatives, that eventually feedback to drive further clinical research (Figure 5).[16] The ultimate goal of course remains the improvement of cardiovascular care to our patients.

Conclusions

Therapeutic approaches to the management of ACS patients continue to evolve rapidly with the publication of multiple landmark trials that have redefined patient care and continual updates of the ACC/AHA practice guidelines for the management of ACS. Despite these

achievements, treatment patterns for these syndromes remain suboptimal, with outcomes seen in randomized clinical trials being unmatched in the "real world" setting. Quality improvement efforts are, therefore, essential to promote increased adherence to guidelines and to overcome the challenges that limit the use of beneficial therapies for ACS. Initiatives are being developed worldwide, however, while there remains no "magic" formula for quality improvement, sustained enthusiasm and flexibility regarding approaches to performance improvement, along with multidisciplinary involvement and ongoing education and feedback, are likely to be critical. These quality-improvement strategies are necessary to promote the use of clinical practice guidelines, thus ensuring sustained improvements in care, and better outcomes for our ACS patients.

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