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Rising to the challenge: transforming the treatment of ST-segment elevation myocardial infarction

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The treatment of ST-segment elevation myocardial infarction has undergone profound changes since the bedrest era of the 1960s. Most recently, the use of percutaneous coronary intervention (PCI) has been shown to be superior to thrombolysis. However, to be effective, PCI must be done as soon as possible after MI. Patients in large urban areas of Canada may have access to PCI, but what about those in most other areas? We asked 2 groups of authors to comment on the gap between evidence and implementation as well as the barriers to round-the-clock PCI capability in Canada and how they can be overcome. The perspective of Madhu Natarajan and Salim Yusuf precedes this comment.

The care of patients with ST-segment elevation myocardial infarction (STEMI) is continually evolving. In the early 1960s, typical care involved primarily bedrest with few, if any, interventions. This was followed by an era of closer observation in coronary care units[1] but still little in the way of beneficial medical interventions apart from prompt cardioversion of lethal arrhythmias. More recently, typical care has evolved to incorporate acute treatment with ASA, heparins, β-blocking drugs, angiotensin-converting-enzyme inhibitors and thrombolytic agents.[2–5] This evolution toward new, efficacious therapies has been accompanied by a decrease over time in the rate of death from myocardial infarction[6] — a good news story.

Many innovations in the treatment of myocardial infarction encountered resistance or delays in uptake. β-Blocking agents were not unanimously endorsed at the outset.[7] Similarly, the use of thrombolytic agents only became a recommended standard of care for STEMI in the late 1980s and early 1990s, about 13–14 years after cumulative analysis of existing trials firmly established its benefit.[8]

The treatment of STEMI is on the verge of evolving yet again in response to a new wave of innovations. At the front of the wave is primary percutaneous coronary intervention (PCI) — or primary angioplasty — a mechanical intervention that re-establishes the patency of infarct-related vessels in the early hours after STEMI. Although findings from the early clinical trials showing benefit of this treatment were viewed with some caution,[9] more recent data from a number of clinical trials summarized in 3 rigorous systematic reviews[10–12] indicate that, for every 1000 cases of STEMI, primary PCI could result in 20 to 30 fewer deaths, about 10 fewer strokes and about 60 fewer patients experiencing a composite end point of stroke, recurrent myocardial infarction or death. Such reductions are quite notable, even after recurrent myocardial infarction (an end point of less clinical significance than stroke or death) is excluded from the composite end point.

PCI could potentially lead to both better patient outcomes and long-term cost savings.

Critics have rightly pointed out that the thrombolytic regimens tested in some of these studies have been suboptimal and that volume-outcome considerations and door-to-angioplasty times for primary PCI in usual care may at least partially attenuate the impressive benefits seen in clinical trials. A second major concern with primary PCI is its relative geographic inaccessibility to some patients owing to the centralization of high-technology care in large urban hospitals. Indeed, with this centralization, implicit trade-offs have had to be made between efficiency and equity. Fortunately, however, these latter concerns have been addressed at least in part by a series of recent clinical trials,[13–15] the results of which suggest that patients with STEMI who present to community hospitals without catheterization facilities do best if transferred immediately to hospitals with such facilities for primary PCI. The magnitude of benefit associated with an immediate-transfer strategy was surprisingly large across studies, with absolute risk reductions of 6% to 15% for the composite end point of death, recurrent myocardial infarction or stroke,[13–15] provided patients were rapidly triaged in the community hospital and transported to a tertiary care centre within 90 minutes. Another approach to overcoming the challenge of geography and access is to develop new PCI facilities in carefully selected hospitals, an approach that Aversano and colleagues[16] have recently proven to be beneficial and feasible in a remarkably short period. Of course, the caveats mentioned earlier regarding suboptimal thrombolytic regimens and feasibility of short door-to-angioplasty times in usual care also apply in the interpretation of results from these trials of immediate-transfer strategies.[13–15]

Economic studies done to date have not factored in the potentially substantial up-front costs of expanding the technological infrastructure for primary PCI or the associated costs of establishing teams of well-trained health care professionals capable of delivering primary PCI in a timely manner. However, early cost-effectiveness studies conducted in centres with existing PCI facilities are encouraging and suggest that, once human resources and expanded technological infrastructures are in place, primary PCI is a "dominant" treatment strategy relative to thrombolysis, with better clinical outcomes and lower costs[17–19] (e.g., mean hospital cost of US$27 700 for primary PCI v. US$30 200 for thrombolysis[17] and, in a recent Canadian study, mean direct hospital cost of Can$10 711 for primary PCI v. Can$13 664 for thrombolysis[19]). These early data therefore suggest that up-front investments to expand the infrastructure for primary PCI could potentially lead to both better patient outcomes and long-term cost savings.

Results from clinical and economic studies of primary PCI have thus been generally very favourable, and one might expect this treatment to consequently be in widespread use across Canada. Yet, this is far from being the case. A recent international study on technological change for the treatment of myocardial infarction reveals that Canada lags behind most countries in the uptake of primary PCI,[20] a finding confirmed by anecdotal reports from cardiac care providers across the country, who have indicated that few centres offer round-the-clock primary PCI. Some centres have begun the shift toward primary PCI by adopting a strategy of PCI by day and thrombolysis by night, or a rescue strategy when thrombolysis has failed. Few, if any, regions have created an immediate transfer network for redirecting cases from community hospitals to PCI centres. The delay in shifting to primary PCI is defensible at least in part because of human resource considerations, initial uncertainty regarding cost-effectiveness and uncertainty regarding optimal strategies for patients presenting to community hospitals. However, the more recent evidence discussed earlier clearly indicates that *now* is the time for cardiac care in Canada to evolve.

There are competing innovations other than primary PCI that merit attention. Most notable is out-of-hospital thrombolysis,[21] an approach that has been shown to shorten the time to thrombolytic administration by 30–60 minutes. However, we suspect that the demonstrated advantage of primary PCI over thrombolysis is unlikely to be due solely to delays in the typical administration of thrombolysis. Another interesting approach is that of "facilitated PCI"[22] — that is, initial treatment with thrombolysis (perhaps in the field before arrival at hospital) followed by rapid transfer to a facility where PCI can be performed. This strategy has the appeal of providing the benefits of both early treatments without the drawbacks of either delayed treatment (a bigger problem with primary PCI) or suboptimal reperfusion (a bigger problem with thrombolysis). However, facilitated PCI requires careful evaluation in randomized controlled

trials before its widespread use can be recommended.

The transfer of high-quality and seemingly definitive evidence into practice is not always easy or timely, but in the case of primary PCI this needs to proceed as rapidly as possible given the impressive data in support of this treatment. To this end, we propose — in an admittedly simplified manner — 3 initial action steps. The first is for cardiac care providers and health care system decision-makers across Canada to embrace the concept of providing primary PCI to increasing numbers of patients, with capacity in tertiary care centres increased to allow for round-the-clock PCI, 7 days a week. The second key step is for system planners to begin assessing the human resource and technological infrastructure needs for primary PCI in their region and to work toward establishing integrated regional cardiac care networks that will link, through improved communication and transportation systems, community hospitals with regional tertiary care centres that have PCI facilities. The third step is for cardiac care providers, researchers and funding agencies to embrace research initiatives addressing issues in acute myocardial infarction care so that we can better understand the optimal approach to facilitating PCI, providing primary PCI and setting up communication and transportation systems to establish efficient cardiac care networks. These early steps will not be simple to achieve; each will require considerable discussion, debate and planning among involved parties.

Nevertheless, the evidence on new and improved treatments for acute STEMI is compelling. Now is the time to move forward to combine the science, the realities of clinical practice, and sound policy into a strategic approach that will provide reasonable access to these new treatments for increasing numbers of Canadians.

This article has been peer reviewed.

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Competing interests: None declared for Drs. Ghali, Donaldson, Lewis, Maxwell or Tu. Dr. Knudtson has received speaker fees from Eli Lilly for lectures on the topic.

Contributors: Dr. Ghali was the principal author and conducted the literature review. Dr. Donaldson contributed to the discussion of economic considerations and priority-setting for primary percutaneous coronary intervention. Drs. Knudtson and Maxwell contributed to the literature review. Dr. Lewis contributed to the discussion of policy considerations. Dr. Tu contributed to the discussion of health care system considerations and utilization issues. All of the coauthors provided critical feedback on successive drafts of the commentary.

Acknowledgements: Drs. Ghali and Tu are supported by Government of Canada Research Chairs in Health Services Research. Drs. Ghali, Donaldson and Maxwell are supported by salary support research awards from the Alberta Heritage Foundation for Medical Research. Drs. Donaldson and Maxwell hold salary support awards from the Canadian Institutes of Health Research.

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