

Regionalization of ST-Segment Elevation Acute Coronary Syndromes Care

Putting a National Policy in Proper Perspective

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A uniform policy for regionalization of ST-segment elevation myocardial infarction (STEMI) care raises several concerns. Transferring all STEMI patients to obtain primary percutaneous coronary intervention (PCI) may be less effective than transferring only high-risk STEMI patients. Delays in time to treatment >60 min associated with transferring patients for primary PCI may result in increased mortality for the average patient as compared with providing immediate fibrinolytic therapy at their initial hospital; yet more than 95% of patients transferred for primary PCI in the U.S. exceed this 60-min benchmark. Superior outcomes associated with treatment at higher-volume regional STEMI centers are inconsistent among centers, and there is no direct evidence that patients will benefit by a transfer to a high-volume hospital from a low-volume hospital. Published data suggest as many as 800 PCI patients would need to be transferred to a high-volume PCI hospital to avoid a single death at a low-volume PCI hospital. Although European randomized trial data suggest transferring patients with STEMI for primary PCI may be superior to immediate fibrinolytic therapy, these findings are unlikely to generalize to the U.S. health care system given size, geography, and organization. ST segment elevation myocardial infarction care regionalization would require a massive redistribution of health care resources, depriving several hospitals of advanced cardiac care facilities, expertise, and associated revenue. Clearer evidence of the benefits and discussion of potential harms are needed before adopting a national STEMI regionalization policy. (J Am Coll Cardiol 2006;47:1346–9) © 2006 by the American College of Cardiology Foundation

However beautiful the strategy, you should occasionally look at the results.

—Winston Churchill (1)

The quality of care provided to patients hospitalized with ST-segment elevation myocardial infarction (STEMI) in the U.S. leaves room for improvement. Recent studies provide evidence of shortfalls in the overall use of guideline-recommended treatment and inappropriate variations in treatment, including by race, gender, geographic location, and time and day of presentation (2–5). Although efforts such as the American College of Cardiology's Guidelines Applied in Practice program have focused on improving the quality of care provided at all hospitals currently treating patients with STEMI, some have suggested that notable improvements require an extensive reconfiguration in the way we provide care for acute coronary syndromes (ACS) in the U.S. (6,7).

Henry et al. (8) offer the most recent version of this approach. Their proposal advocates a national policy modeled on trauma care whereby patients with STEMI would be routed directly to designated STEMI centers, potentially bypassing closer centers. Improving the treatment of STEMI is a laudable goal. Nevertheless, we remain troubled by the lack of robust data supporting such a sweeping change in clinical practice and the continued lack of attention paid to the practical implications of this approach (9). In this paper, we explain why the claimed benefits of STEMI regionalization may not be realized and present potential unintended harms that may be associated with such a policy.

Claim 1: primary percutaneous coronary intervention (PCI) is superior to fibrinolytic therapy for all patients. Although primary PCI may yield better clinical outcomes than fibrinolytic therapy when delivered promptly and at experienced centers (10), a large number of patients may not accrue this benefit. A study of 10 trials of reperfusion therapy indicated that focusing the use of primary PCI on those approximately 40% of patients at highest risk would achieve similar outcomes to treating all patients with primary PCI (11). More recent data suggest that the incremental benefit of primary PCI is modified by patient risk, with no benefit for primary PCI as compared with fibrinolytic therapy in the large number of patients who are at low risk (12). As such, a primary PCI-only strategy may have negative consequences for lower-risk patients. These pa-

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Abbreviations and Acronyms

ACS	= acute coronary syndromes
EMS	= emergency medical services
PCI	= percutaneous coronary intervention
STEMI	= ST-segment elevation myocardial infarction

tients are unlikely to achieve a substantive improvement in outcomes with primary PCI compared with fibrinolysis, yet may incur an increased risk because of the delay required for transfer to primary PCI-capable centers. Further, patients treated within the first 2 to 3 h of symptom onset may achieve comparable outcomes with fibrinolytic therapy as with primary PCI, on average (13,14). Given the continued evolution of adjuvant and fibrinolytic therapies (15) and initial results with pre-hospital fibrinolytic treatment, there will be a continued need to assess the utility of different fibrinolytic treatment regimens compared with primary PCI. In the interim, a more pragmatic approach would focus on treating with primary PCI those STEMI patients who are most likely to benefit or are ineligible for fibrinolytic therapy, rather than implementing a “one size fits all” policy.

Transferring patients to regional STEMI centers or bypassing closer hospitals capable of providing fibrinolytic therapy will increase time to treatment. Even among patients undergoing primary PCI, delays to reperfusion are associated with an increased risk of in-hospital and long-term mortality (16). Although published studies of transfer indicate that the absolute rate of ventricular arrhythmia or death is <2% during transfer, this estimate may not be generalizable given the small numbers and selected nature of randomized controlled trial populations. In the real world, it will likely be higher due to longer transfer times and sicker patient populations.

Even more concerning is the absence of discussion regarding how much additional delay in treatment is acceptable to obtain primary PCI in patients who are eligible for immediate fibrinolytic therapy. Work by Nallamothu and Bates (17) suggests that the incremental benefit of primary PCI over fibrinolytic therapy noted in randomized controlled trials may be negated when delays for primary PCI exceed the time it would take to deliver fibrinolytic therapy by 60 min. Thus, in order for admissions to regional STEMI centers in lieu of nearest available facilities to be effective, the total time from the door of the first hospital to initial balloon inflation during PCI at the second hospital should not be more than 90 min—or 60 min longer than the 30 min typically required to deliver fibrinolytic therapy at the first hospital. Data from the National Registry of Myocardial Infarction-2 and -3, however, report that patients undergoing interhospital transfer for PCI in the U.S. experience a median time from presentation at the first hospital to PCI at the second hospital of 180 min (18). In fact, fewer than 5% of interhospital transfers in the U.S.

occur within 90 min (18). Thus, for patients who have no contraindications to fibrinolysis and would incur a substantial treatment-associated delay, prompt fibrinolysis at the closest available hospital will do as much or more to maximize outcomes than would transfer to a regional ACS center.

Claim 2: directing patients to ACS centers with higher volume, more specialists, and more intensive treatment will improve their outcomes. There are limited data regarding the association between hospital STEMI volume and outcomes. Proponents of STEMI regionalization have relied instead on studies of hospital PCI volume and outcomes to suggest that restricting STEMI patients to higher-volume PCI centers will improve outcomes. Although higher-volume PCI centers have superior outcomes compared with lower-volume PCI centers (19), recent studies suggest hospital PCI volume is a poor marker for individual hospital PCI outcomes (20). Hospital PCI volume-associated differences in mortality have decreased in the past 20 years, and overall differences in mortality between high- and low-volume PCI centers are negligible (21). We are not aware of any studies that experimentally evaluate whether shifting patients from low-volume PCI centers to high-volume PCI centers improves outcomes. A study using administrative data assessed the national impact of transferring all PCI procedures from hospitals performing fewer than 200 PCI cases annually to hospitals with more than 200 annual PCI cases. In a best-case scenario, in which transferred patients obtain the superior outcomes of the receiving hospital, more than 800 patients would have to be transferred from low-volume PCI hospitals to avoid a single death (22). Regardless, the success of a large-scale implementation would depend on several untested assumptions, including the comparability of patients across low- and high-volume hospitals, the ability of hospitals to tolerate large-volume increases and maintain their performance, and the “transferability” of volume effects across hospitals.

Increasing access to cardiovascular specialty care and more intensive treatments may have limited benefits. Policies that endorse universal access to primary PCI at regional STEMI centers disregard reports of superior outcomes for patients treated in collaborative care models using generalist and specialist physicians (23). Specialty care itself may lead to more intensive treatment patterns that may not necessarily result in improved outcomes, but would drive up costs. For instance, ACS patients treated in areas with higher rates of invasive management have outcomes comparable to those of patients treated in regions with lower rates of invasive management but optimal medical care (24). Promoting the spread of intensive, interventional management of ACS, as would likely occur in specialty-managed patients or at designated STEMI centers, belies the fact that many patients may not need nor even benefit from such treatment (25).

Claim 3: European-based studies of transferring patients for primary PCI are generalizable to the U.S. Evidence supporting the benefits of transferring patients for primary

PCI is based on the results of five randomized controlled trials conducted primarily in Europe (13,26-29). In addition to excluding patients who would not be suitable for transport, these studies were conducted in small geographic regions with centralized hospital systems. In contrast, populations in the U.S. are more dispersed, emergency medical services (EMS) more heterogeneous, and most hospitals are not directly government-administered. These differences lead us to suggest caution in applying these results to the U.S.

Of greater concern is the lack of any direct data concerning transferring patients for STEMI from populations in the U.S. The only study of transfer to enroll patients in the U.S. was the Randomized Trial of Transfer for Primary Angioplasty Versus On-site Thrombolysis in Patients with High-Risk Myocardial Infarction (Air-PAMI), and it enrolled only 83 patients with STEMI over a three-year period, or approximately one patient every four months, at its nine participating centers (28). This population represents <0.02% of the estimated 500,000 patients hospitalized for STEMI in the U.S. in any given year (30). It is clear that a more robust, generalizable evidence base is needed before implementing regionalization of STEMI care across the entire U.S.

Claim 4: STEMI regionalization can be organized like a level 1 trauma system. There are two major differences between trauma and STEMI care that undermine this analogy. First, the scale of STEMI care in terms of both the numbers of patients affected and the resources needed is much larger than for trauma care. Regionalizing STEMI care delivery would involve shifting resources on a massive scale. Such a strategy would also require developing capacities that are still experimental. Field-based electrocardiogram testing, a key component of the proposed system, has produced mixed results in limited studies and remains untested on a national scale (31,32). Moreover, unlike trauma, ACS patients often present to the hospital directly, bypassing EMS. In addition, even if such patients were to use EMS, the diagnosis of STEMI or ACS is not always clear: more than 80% of patients with symptoms suggestive of ACS are not found to be experiencing acute cardiac ischemia, let alone STEMI (33). Given that there is a trend for an increasingly smaller proportion of patients with ACS to develop STEMI (34), regional ACS centers that directly receive symptomatic patients may find themselves swamped by non-cardiac cases and patients with non-ST-segment elevation infarctions.

The difference in scale between ACS and trauma care implies that regionalizing STEMI care would be much more expensive and resource-intensive than it has been for trauma. Not only would the up-front costs to reconfigure STEMI care nationwide be exorbitant, but the ongoing costs would be substantial as well. In particular, regionalization would impose a heavy burden on EMS providers, who would be responsible for transporting the large numbers of suspected STEMI patients for primary PCI. The adoption of STEMI regionalization and its associated

demands for transfer to STEMI centers would likely require either the expansion of current EMS capacity or reductions in the availability of EMS for other needs.

Second, cardiovascular care, unlike trauma, is a financially attractive service for hospitals. For hospitals that provide them, cardiac procedures account for some 35% of total hospital revenue on average (35), and that revenue is frequently needed to cross-subsidize other hospital services. It is therefore not surprising that acute care general hospitals have sought to prevent the entry into their markets of cardiac specialty hospitals, which, like regional ACS centers, threaten to take valued cardiac procedure volume and associated revenues. Although both cardiovascular and trauma services require substantial capital investments, trauma services are not a notable source of hospital revenue.

A system of designated STEMI centers would reinforce the division between the cardiac “haves” and the “have nots.” It would be naive to think that hospitals not receiving a regional STEMI center designation would willingly send their STEMI patients elsewhere. Policy makers should expect that the potential losers will resist regionalization under the current reimbursement system. Moreover, we are not optimistic that the adjustments to reimbursement envisioned by Henry et al. (8) will be sufficient to address these hospitals’ concerns. The threat of being left out under regionalization may provide the necessary incentive for hospitals to preemptively seek to satisfy criteria that may earn them designation as regional STEMI centers, possibly including opening new cardiac catheterization labs or expanding capacity in existing labs. In states without Certificate of Need regulation, there is little to prevent this from happening. A restrictive nationwide STEMI regionalization policy could collide with federal regulatory objectives, which favor policies that promote, not inhibit, hospital competition. The U.S. Federal Trade Commission and the Department of Justice recently recommended, for example, that “states should decrease barriers to entry into provider markets” (36). The assertion by Henry et al. (8) that sufficient numbers of cardiologists will willingly staff non-STEMI hospitals is similarly naive. This was made clear in a recent Connecticut Certificate of Need application in which a center petitioning for primary PCI services justified its request, in part, on its need to recruit and retain cardiovascular specialists (37).

Conclusions. Several issues merit consideration in the discussion of regionalized STEMI care. Current evidence for the purported benefits of regionalizing STEMI care has limitations, including limited applicability to the U.S. health care system and no direct data that transferring patients from low-volume PCI centers to high-volume PCI centers reduces mortality. Hospital size, technology, and specialty care do not guarantee high-quality STEMI care, just as the absence of these factors does not preclude quality care. Absent from discussion of the proposed policy are the potential problems that may accompany regionalization, including feasibility, risks to patients, and the health care

system. Although STEMI care regionalization has its proponents, the current data are insufficient to endorse such a fundamental change in the health care system. Clear compelling evidence of the benefits of STEMI care regionalization and a better understanding of its potential consequences within the U.S. are needed before implementing any such national policy.

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REFERENCES

- Churchill W. Available at: <http://www.quotedb.com/quotes/3460>. Accessed February 6, 2006.
- Vaccarino V, Rathore SS, Wenger NK, et al. Sex and racial differences in the management of acute myocardial infarction, 1994 through 2002. *N Engl J Med* 2005;353:671-82.
- Magid DJ, Wang Y, Herrin J, et al. Relationship between time of day, day of week, timeliness of reperfusion, and in-hospital mortality for patients with acute ST-segment elevation myocardial infarction. *JAMA* 2005;294:803-12.
- Jencks SF, Cuedon T, Burwen DR, et al. Quality of medical care delivered to Medicare beneficiaries: a profile at state and national levels. *JAMA* 2000;284:1670-6.
- Rathore SS, Masoudi FA, Havranek EP, Krumholz HM. Regional variations in racial differences in the treatment of elderly patients hospitalized with acute myocardial infarction. *Am J Med* 2004;117:811-2.
- Califf RM, Faxon DP. Need for centers to care for patients with acute coronary syndromes. *Circulation* 2003;107:1467-70.
- Topol EJ, Kereiakes DJ. Regionalization of care for acute ischemic heart disease: a call for specialized centers. *Circulation* 2003;107:1463-6.
- Henry TD, Atkins JM, Cunningham MS, et al. ST-segment elevation myocardial infarction: recommendations on triage of patients to heart attack centers: is it time for a national policy for the treatment of ST-segment elevation myocardial infarction? *J Am Coll Cardiol* 2006;47:1339-45.
- Rathore SS, Epstein AJ, Volpp KGM, Krumholz HM. Regionalization of care for acute coronary syndromes: more evidence is needed. *JAMA* 2005;293:1383-7.
- Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet* 2003;361:13-20.
- Kent DM, Schmid CH, Lau J, Selker HP. Is primary angioplasty for some as good as primary angioplasty for all? Modeling across trials and individual patients. *J Gen Intern Med* 2002;17:887-94.
- Thune JJ, Hoefsten DE, Lindholm MG, et al. Simple risk stratification at admission to identify patients with reduced mortality from primary angioplasty. *Circulation* 2005;112:2017-21.
- Widimsky P, Budesinsky T, Vorac D, et al. Long-distance transport for primary angioplasty vs immediate thrombolysis in acute myocardial infarction: final results of the randomized national multicentre trial—PRAGUE-2. *Eur Heart J* 2003;24:94-104.
- Steg PG, Bonnefoy E, Chabaud S, et al. Impact of time to treatment on mortality after prehospital fibrinolysis or primary angioplasty: data from the CAPTIM randomized clinical trial. *Circulation* 2003;108:2851-6.
- Sabatine MS, Cannon CP, Gibson CM, et al. Addition of clopidogrel to aspirin and fibrinolytic therapy for myocardial infarction with ST-segment elevation. *N Engl J Med* 2005;352:1179-89.
- De Luca G, Suryapranata H, Ottervanger JP, Antman EM. Time delay to treatment and mortality in primary angioplasty for acute myocardial infarction: every minute of delay counts. *Circulation* 2004;109:1223-5.
- Nallamothu BK, Bates ER. Percutaneous coronary intervention versus fibrinolytic therapy in acute myocardial infarction: is timing (almost) everything? *Am J Cardiol* 2003;92:824-6.
- Nallamothu BK, Bates ER, Herrin J, et al. Times to treatment in transfer patients undergoing primary percutaneous coronary intervention in the United States: National Registry of Myocardial Infarction (NRFMI) 3/4 analysis. *Circulation* 2005;111:761-7.
- Canto JG, Every NR, Magid DJ, et al. The volume of primary angioplasty procedures and survival after acute myocardial infarction. *N Engl J Med* 2000;342:1573-80.
- Epstein AJ, Rathore SS, Volpp KGM, Krumholz HM. Hospital percutaneous coronary intervention volume and patient mortality, 1998 to 2000: does the evidence support current procedure volume minimums? *J Am Coll Cardiol* 2004;43:1755-62.
- Ho V. Evolution of the volume-outcome relation for hospitals performing coronary angioplasty. *Circulation* 2000;101:1806-11.
- Epstein AJ, Rathore SS, Krumholz HM, Volpp KGM. Volume-based referral for cardiovascular procedures in the United States: a cross-sectional regression analysis. *BMC Health Serv Res* 2005;5:42.
- Ayanian JZ, Landrum MB, Guadagnoli E, Gaccione P. Specialty of ambulatory care physicians and mortality among elderly patients after myocardial infarction. *N Engl J Med* 2002;347:1678-86.
- Stukel TA, Lucas FL, Wennberg DE. Long-term outcomes of regional variations in invasive versus medical management of Medicare acute myocardial infarction patients. *JAMA* 2005;293:1329-37.
- Bogaty P, Brophy J. Increasing burden of treatment in the acute coronary syndromes: is it justified? *Lancet* 2003;361:1813-6.
- Andersen HR, Nielsen TT, Rasmussen K, et al. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. *N Engl J Med* 2003;349:733-42.
- Widimsky P, Groch L, Zelizko M, et al. Multicentre randomized trial comparing transport to primary angioplasty vs immediate thrombolysis vs combined strategy for patients with acute myocardial infarction presenting to a community hospital without a catheterization laboratory. *Eur Heart J* 2000;21:823-31.
- Grines CL, Westerhausen DR, Grines LL, et al. A randomized trial of transfer for primary angioplasty versus on-site thrombolysis in patients with high-risk myocardial infarction: the Air Primary Angioplasty in Myocardial Infarction study. *J Am Coll Cardiol* 2002;39:1713-9.
- Vermeer F, Ophuis AJM, vd Berg EJ, et al. Prospective randomized comparison between thrombolysis, rescue PTCA, and primary PTCA in patients with extensive myocardial infarction admitted to a hospital without PTCA facilities: a safety and feasibility study. *Heart* 1999;82:426-31.
- Antman EM, Anbe DT, Armstrong PW, et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of Patients With Acute Myocardial Infarction). *J Am Coll Cardiol* 2004;44:e1-e211.
- Otto LA, Aufderheide TP. Evaluation of ST segment elevation criteria for the prehospital electrocardiographic diagnosis of acute myocardial infarction. *Ann Emerg Med* 1994;23:17-24.
- Feldman JA, Brinsfield K, Bernard S, White D, Maciejko T. Real-time paramedic compared with blinded physician identification of ST-segment elevation myocardial infarction: results of an observational study. *Am J Emerg Med* 2005;23:443-8.
- Pope JH, Aufderheide TP, Ruthazer R, et al. Missed diagnoses of acute cardiac ischemia in the emergency department. *N Engl J Med* 2000;342:1163-70.
- Rosengren A, Wallentin L, Simoons ML, et al. Cardiovascular risk factors and clinical presentation in acute coronary syndromes. *Heart* 2005;91:1141-7.
- Devers KJ, Brewster LR, Ginsburg PB. Specialty Hospitals: Focused Factories or Cream Skinners? Washington, DC: Center for Studying Health System Change, 2003.
- Improving Health Care: A Dose of Competition. Washington, DC: US Federal Trade Commission and US Department of Justice, 2004. Available at: <http://www.ftc.gov/reports/healthcare/040723healthcarerpt.pdf>. Accessed February 7, 2006.
- Norwalk hospital certificate of need application to establish an interventional cardiology and cardiac surgery program, Connecticut Office of Health Care Access, Hartford, CT (2005) (prefiled testimony of Eric Mazur, MD).