EDITORIAL COMMENT

Old Age, Left Bundle Branch Block and Acute Myocardial Infarction: A Vexing and Lethal Combination*

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The evolution of reperfusion therapy in the treatment of acute myocardial infarction (AMI) has highlighted the extraordinary importance of rapid and accurate diagnosis of infarcts due to thrombosis of a major epicardial vessel, the so-called Q-Wave Myocardial Infarction or Transmural Myocardial Infarction. The presence of AMI can be established by a wide variety of diagnostic tests, but the narrow temporal window for significant myocardial salvage with reperfusion dictates that the clinical presentation and the 12-lead ECG remain the principal tools available to make the decision about reperfusion therapy. Although reperfusion therapy has been embraced enthusiastically for treatment of all ST segment elevation AMI, the benefit is greatest in those subsets of patients with the highest absolute risk for mortality, anterior myocardial infarction and subsets of inferior infarction and other locations (1,2). In subsets of very-low-risk infarcts, mortality benefit for reperfusion therapy is marginal or has not been demonstrated (3).

Age is a powerful determinant of outcome (4−7). The mortality risk of AMI increases almost logarithmically with age and 70% of fatal infarcts occur in patients over the age of 65 years. These well-known features concerning AMI and reperfusion therapy make the observational study of Shlipak et al. (8), concerning the treatment and outcomes of left bundle branch block (LBBB) in patients with AMI reported in this issue of the Journal, of particular interest.

Regardless of the changes and improvements in the logistics of therapy in AMI, better outcomes will always be contingent on prompt recognition of the patients who are candidates for reperfusion therapy, particularly those at high risk.

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The current study. The National Registry of Myocardial Infarction 2 (NRMI-2) is a voluntary prospective observational registry of 772,586 patients with AMI admitted to 1,470 hospitals in all 50 states in the U.S. (8). The data were collected between 1994 and 1998. This rich database describes contemporary practice and provides information on an extraordinary subset of 29,585 patients with LBBB and AMI. This huge sample of LBBB patients constitutes 3.7% of the total NRMI-2 infarct population. In keeping with the fact that LBBB is often associated with large anterior myocardial infarctions and the mean age of these patients was 76.4 years, the mortality rate of 22%, was extremely high. Other notable attributes of the sample include a high prevalence of major co-morbidity; congestive heart failure in nearly 40%, diabetes in 37% and hypertension in over half of the sample population. Not surprising in light of the advanced age, half of the sample population were female in contrast to the gender mix in younger subsets of AMI in which male patients predominate.

A particularly important feature is the extremely low utilization of reperfusion therapy; only 8.4% of the sample population had any form of reperfusion. Since the absolute benefit (e.g., number needed to treat to prevent one death or number of lives saved per thousand patients treated) of reperfusion therapy is greatest in the infarcts of highest risk, this is a particularly disturbing characteristic of contemporary practice. The investigators’ analyses provide important explanations for the phenomenon of failure to treat. Nearly half of the patients (47%) presented without chest pain. The absence of chest pain (ischemic discomfort) is a frequent feature in elderly patients with AMI (9–12). Although no data related to the actual presenting complaints are given, it is reasonable to assume that the majority had dyspnea, the common presenting complaint in elderly patients with AMI.

The combination of a nondiagnostic ECG (LBBB) and the absence of chest pain undoubtedly discouraged the use of reperfusion therapy in this very high-risk population. An extremely small proportion, 2.6%, without chest pain received reperfusion therapy. However, only 13.6% of patients with chest pain received reperfusion therapy. Other treatment and diagnostic procedures were used significantly less often in the non–chest pain group: aspirin, 73% versus 55%; beta-blocker, 33% versus 18%; heparin, 69% versus 48%; elective coronary arteriography, 33% versus 16%; elective percutaneous transluminal coronary angioplasty, 12% vs. 4%; and elective coronary artery bypass; 6% vs. 3%. Only angiotensin-converting enzyme inhibitors were used with equal frequency (30% vs. 32%). Left bundle branch block was found in 2.7% of patients with AMI <65 years of age and in 10.5% in those >75 years old. In the LBBB-AMI group, 37% <65 years presented with chest pain, while 50% of those >75 years had no chest discomfort.

In a larger context, the LBBB-AMI group reflects the
Clinical issues in the old age group with AMI; namely, presenting complaints tend to be atypical and ECG findings tend to be nondiagnostic. A frequent ECG finding is ST segment depression with the development of non-Q-wave infarct (13). As confirmed by this report, these “atypical” features (for young patients!) do not connote a lower mortality rate in the elderly. We must improve our recognition of the clinical presentation of AMI in the elderly; “atypical” presentations in reference to symptoms and ECG findings should be considered frequent and the norm. The clear message from the work of Shlipak et al. (8) is the need to lower the diagnostic threshold for considering AMI when LBBB is present, especially in the older patient.

**Can AMI be diagnosed by ECG when LBBB is present?**

Better tests for AMI that can be immediately available in the emergency department are being intensively investigated but, in the near future, the 12-lead ECG will remain the primary diagnostic tool to assess the presence of epicardial coronary arterial thrombosis and make the decision for reperfusion therapy.

With LBBB, the course of ventricular activation is altered, which secondarily affects ventricular repolarization. The QRS, ST-segment and T wave of the ECG are always affected by LBBB. More often than not, the early signs of AMI will be obscured by the changes due to the conduction abnormality. The prevalence of LBBB and other cardiac conduction abnormalities increases with age. While LBBB due to “sclerodegenerative” disease (14–16) or senile amyloidosis (17) can occur in the absence of other structural heart disease or cardiac symptoms (18), detailed clinicopathologic studies (14–17) show that LBBB increases in the elderly and is more often associated with advanced cardiac disease of several types. Thus, LBBB is a marker both of age and severe heart disease but not exclusively coronary disease.

Multiple studies have evaluated the ability to diagnose AMI when LBBB is present (19–24). The work of Sgarbossa et al. (24) is instructive in this regard. They developed diagnostic criteria for AMI when LBBB was present using data from the GUSTO-1 Trial (the derivation or training sample) and from a control population with LBBB and stable ischemic heart disease (the validation sample). Three ECG criteria based on ST segment displacement were found to have independent diagnostic value (see legend of the Fig. 1). The three criteria were assigned index scores and incorporated in a diagnostic algorithm. This algorithm was found to have a sensitivity of 78% and a specificity of 90% in the derivation/training sample. The diagnostic specificity remained high, 96%, but the sensitivity was quite low, 36%, when applied to the validation sample, a small group of 45 patients. In an earlier report, Shlipak et al. (25) tested the Sgarbossa algorithm and other ECG criteria for myocardial infarctions in patients with LBBB and found that none effectively distinguished the patients with myocardial infarction from those with other diagnoses. A possible explanation for these differing results is that the Sgarbossa algorithm was derived and validated in a cohort of patients with LBBB from the GUSTO-1 Trial, which represented only 0.5% of the 26,003 patients enrolled in the trial (26). This low percentage of LBBB in AMI suggests that the cohort studied by Sgarbossa et al. (24) was highly selected and may not be representative of the universe of patients with this combination of abnormalities.

The reported studies of LBBB-AMI suggest that an unknown, albeit small, subset of patients have ECG changes that are indicative of AMI and in this group these findings could lead to immediate fibrinolytic therapy. More research is needed to confirm, refine and determine the frequency of ECG findings of LBBB that may indicate AMI. For example, included in such studies would be the evaluation of serial ECGs, taken over a brief period of 30 to 40 min, to determine if fluctuating repolarization changes may enhance the sensitivity of the 12-lead ECG since repolarization changes are dynamic during the early course of transmural myocardial infarction.

**What might be done to resolve this issue?** No simple approach to resolution is feasible. What can be done immediately and what must be done in order to provide better care is to have a much lower threshold for the suspicion of AMI in all elderly patients with nonspecific cardiac complaints, particularly dyspnea, but with a wide variety of complaints, which are common in AMI in the elderly. When LBBB is present, the suspicion of AMI should be increased, efforts should be made to obtain previous ECGs and particular attention should be paid to subtle changes in repolarization, which will lead to more definitive tests.

In patients in whom the suspicion of AMI is high, reperfusion therapy should be seriously considered because of the high mortality of AMI-LBBB in elderly patients. Obviously, a highly individualized approach is needed with careful consideration of the patient’s general health activity status and co-morbidity (26). If fibrinolytic therapy is selected, streptokinase has been demonstrated in all studies to have a lower risk of cerebral hemorrhage—the most dreaded complication of therapy—which increases in the elderly population (27,28). In addition, decision analysis using the GISSI-1 database has demonstrated fibrinolysis to be cost effective even when the probability of diagnosis of AMI is relatively low in elderly patients because the mortality is so high and the mortality benefit was great (33% to 29% reduction) (29).

In patients with LBBB in whom the diagnosis is probable but not certain, emergency cardiac catheterization both for diagnosis and to plan management is justified. Achieving immediate reperfusion with a catheter-based intervention in this setting is almost certainly more effective than thrombolytic therapy and avoids the risk of central nervous system (CNS) hemorrhage. The NRMI-2 registry emphasizes the approach that could be utilized to clarify the problem. Registries are powerful tools to assess these issues. A large registry of patients with LBBB who are evaluated in
Emergency departments with a variety of complaints could constitute the study sample. The protocol for such a study would include clinical presentation, ECG findings (particularly study of serial ECGs) and the management selected, as well as outcomes. As in any good registry study, definitions would have to be agreed on and used in a prescriptive fashion.

The Venn diagram (Fig. 1) provides a framework to discuss the multiple facets of the problem and management approaches. It is not intended to be prescriptive but to emphasize the fact that multiple permutations exist that call for fastidiously collected data to better define management strategies. If the Sgarbossa criteria were confirmed, patients in subsets A, B and C would proceed to revascularization. Subsets D, E and F pose the dilemma emphasized in the text. If the Sgarbossa criteria were confirmed but the data presented further emphasizes the need for fastidiously collected data to better define management strategies. With the gross underutilization of reperfusion therapy in the elderly population with AMI, the registry method should be used and could help unravel difficult management problems. With >70 million baby boomers soon to enter old age, the issues brought into focus by Shlipak et al. (8) and commented on in this editorial will become even more pressing.

Addendum. A recent publication, (Thieman DR, Coresh J, Schulman S, et. al. Lack of benefit of intravenous thrombolyis in patients with myocardial infarction who are older than 75 years, Circulation 2000;101:2239–2246 2000) reports the lack of benefit and potential adverse effects of fibrinolytic therapy in 7,864 Medicare patients, age 65 to 86 years, with the primary discharge diagnosis of acute myocardial infarction. This observational study needs to be confirmed but the data presented further emphasizes the complexities of the issues involved in elderly patients with acute myocardial infarction and makes catheter-based reperfusion procedures, as discussed in this editorial, more appealing.

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