Association of Unstable Angina Guideline Care With Improved Survival

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Background: An unstable angina guideline was published in 1994 by the Agency for Health Care Policy and Research, Bethesda, Md. However, the relationship between guideline-concordant care and patient outcomes is unknown.

Objective: To determine whether guideline-concordant care is associated with improved outcomes.

Methods: The study sample consisted of 275 consecutive nonreferral patients hospitalized with primary unstable angina. One-year survival and survival free of myocardial infarction were compared between patients who received care concordant with 8 selected guideline recommendations and patients who received discordant care.

Results: Care concordant with the 8 key guideline recommendations was associated with improved 1-year survival (95% vs 81%; log-rank $P<.001$) and survival free of myocardial infarction (91% vs 74%; $P<.001$), compared with guideline-discordant care. Patients in high-risk subgroups had the largest survival benefit associated with guideline-concordant care (aged $\geq 65$ years, 91% vs 74% [ $P=.005$]; heart failure at presentation, 91% vs 68% [ $P=.10$]). Aspirin therapy was the single recommendation most strongly associated with improved 1-year survival (94% vs 78%; $P=.002$).

Conclusions: Care as outlined in the unstable angina clinical practice guideline is associated with improved 1-year outcomes. Subgroups of patients at highest risk and recommendations firmly based on randomized clinical trial data were most strongly associated with better outcomes. These findings support the use of an evidence-based approach to guideline development and assessment of quality of care in patients with primary unstable angina.

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IN 1994, THE Agency for Health Care Policy and Research (AHCPR) released guidelines on the diagnosis and management of unstable angina,1 a diagnosis that leads to at least 1 million hospitalizations per year in the United States.2 The individual recommendations in the guideline were based on randomized, controlled trial evidence or other available evidence for net clinical benefit. Data on long-term outcomes in patients with unstable angina are available from a few published registries3-5 and patient follow-up in clinical trials.5-7 However, data are sparse regarding the association of concordance with guideline recommendations and outcomes in a general population of hospitalized patients.8 We recently reported on a new, simple method for evaluating the AHCPR guideline in patients hospitalized with unstable angina.9 We herein have extended this investigation to examine the relationship between treatment concordant with guideline care and 1-year outcomes.

BASELINE CHARACTERISTICS AND CONCORDANCE

The mean (± SD) age of the 275 study patients was 66 ± 12 years (range, 30-93 years), and half had a history of myocardial infarction. Baseline patient characteristics are shown in Table 2, according to whether care was concordant or discordant with the 8 guideline recommendations. Patients whose care was discordant with the guideline were more likely to be older and to have a history of heart failure, heart failure at presentation in the emergency department, a modified Charlson comorbidity index of 2 or greater, and renal insufficiency (serum creatinine level, $>133 \mu$mol/L [>1.5 mg/dL]).

For each individual recommendation, concordance ranged from 69% (for the appropriate referral for coronary artery bypass surgery recommendation) to greater than 99% (for the no intravenous...
SUBJECTS AND METHODS

PATIENT SELECTION

Details of the patient selection have been described elsewhere.9,10 Briefly, we screened all adults admitted from the emergency department to the coronary or medical intensive care units or cardiac telemetry unit of a large, urban teaching hospital for 1 year. We identified 414 nonreferral patients with unstable angina, as defined by the AHCPR Unstable Angina Clinical Practice guideline.1 We excluded 134 patients with precipitants (eg, sepsis, gastrointestinal tract hemorrhage), high risk for mortality (eg, metastatic cancer), or both, because the guideline recommends individualized care for such patients. Five patients who died before discharge were also excluded from the primary survival analyses, since a complete evaluation of 3 of the guideline recommendations is not possible for patients who died in hospital. Thus, the final cohort for this analysis consisted of 275 consecutive patients with primary unstable angina who survived hospitalization.

BASELINE AND OUTCOMES

DATA COLLECTION

Data were collected on the study patients regarding demographics; baseline cardiovascular risk factors; presenting clinical characteristics (anginal symptoms, noncardiac diagnoses, physical examination findings); results of electrocardiography, x-rays, and laboratory evaluations; cardiac medications; and in-hospital and 1-year outcomes. For each patient we calculated a modified Charlson comorbidity index11 (modified because of the exclusion from the guideline of patients with metastatic cancer or acquired immunodeficiency syndrome). The Charlson index is a widely used research tool that provides risk-adjusted, short-term mortality based on differential weighting of 16 major diagnoses, to assess noncardiac comorbidity. The primary outcome of interest was postdischarge 1-year mortality. The secondary outcome was the occurrence of death or postdischarge myocardial infarction through 1 year. One-year mortality and myocardial infarction data were obtained first from hospital records. Patients with incomplete follow-up were then contacted by mail and telephone. When mortality status remained uncertain, searches of the Massachusetts Death Registry and the Social Security Death Index were performed. Vital status at 1 year was available for all but 1 patient who was a non-US citizen. Complete data on postdischarge myocardial infarction were unavailable for 8 patients. This research project was approved by the Subcommittee on Human Studies at our institution.

DETERMINATION OF GUIDELINE-CONCORDANT CARE

From the 95 recommendations of the AHCPR guideline, we selected 8 that had strong scientific evidence to support them and could be assessed reliably by review of the medical record. Seven of these 8 recommendations were completely or in part grade A (ie, highest-level quality of supporting evidence), whereas the evidence supporting the recommendation to initiate β-blocker therapy at presentation was judged by the guideline as grade B (Table 1). For each of the 8 selected recommendations, concordance with guideline care was determined according to the a priori criteria outlined in Table 1. For the recommendation regarding cardiac catheterization, we used the guideline-specified conservative approach (ie, that patients should be referred for catheterization if they exhibit 1 or more high-risk features). Thus, patients without a high-risk feature were not considered eligible for the catheterization guideline recommendation analysis. To determine overall percentage of concordance for a given recommendation, the number of eligible patients who received the recommended care was divided by the number of patients who were eligible for that recommendation.

For each patient, the percentage of guideline recommendations followed was determined by calculating a concordance score as follows: the number of recommendations for which a given patient was eligible and for which the patient received the recommended care was divided by the number of recommendations for which that patient was eligible. Patients with a concordance score of at least 80% were considered to have received guideline-concordant care. Those with a concordance score of below 80% were considered to have had guideline-discordant care.

STATISTICAL ANALYSIS

Baseline characteristics were compared between patients whose care was guideline concordant and those whose care was guideline discordant, using the t test for continuous variables and the Fisher exact test (from the 2 × 2 contingency tables) for categorical variables. Logistic regression was used to determine multivariate predictors of guideline-discordant care.

Kaplan-Meier survival curves were generated for the primary and secondary end points for each guideline recommendation individually, and for overall guideline-concordant or guideline-discordant care. Using the log-rank test, survival curves were compared between patients who received concordant or discordant care. Cox proportional hazards models were constructed to evaluate predictors of 1-year survival and survival free of myocardial infarction.

We previously demonstrated that older age (per decade) and the presence of congestive heart failure at presentation were the 2 significant multivariate predictors of guideline-discordant care in this study sample.9 Both covariates were also significant univariate predictors of postdischarge 1-year mortality and postdischarge death or myocardial infarction. Given the limited number of outcome events (25 deaths, 10 nonfatal myocardial infarctions), we chose to focus only on these 2 covariates in our secondary analyses. Therefore, bivariate survival analyses were performed to explore the impact of guideline-discordant care in older patients and in patients with congestive heart failure at presentation. For the purposes of the bivariate analyses, age was treated as a dichotomous variable, with older age defined as at least 65 years of age. All statistical analyses were performed using SAS for Windows version 6.11 (SAS, College Station, Tex).
Table 1. Definitions of 8 Important Guideline Recommendations and Potentially Eligible Patients°

<table>
<thead>
<tr>
<th>Guideline (Grade)</th>
<th>Eligible Patients</th>
<th>Criteria for Concordance</th>
</tr>
</thead>
<tbody>
<tr>
<td>No intravenous thrombolytic therapy (A)</td>
<td>All except those with left bundle-branch block on presenting ECG</td>
<td>No administration of intravenous thrombolytic agent for presenting ischemic episode</td>
</tr>
<tr>
<td>Initial aspirin therapy (A)</td>
<td>All except those with aspirin allergy, active bleeding, or high risk for bleeding, as defined by the guideline</td>
<td>Administration of aspirin within 24 h after presentation</td>
</tr>
<tr>
<td>Initial heparin therapy (A)</td>
<td>All except those with heparin allergy, active bleeding, or high risk for bleeding, as defined by the guideline</td>
<td>Administration of intravenous heparin within 24 h after presentation</td>
</tr>
<tr>
<td>Initial β-blocker therapy (B)</td>
<td>All except those with bradycardia, hypotension, or severe LV dysfunction with history of CHF, as defined by the guideline</td>
<td>Administration of β-blocker within 24 h after admission</td>
</tr>
<tr>
<td>Avoidance of calcium channel blockers (A/B)</td>
<td>All except those with systolic blood pressure &gt;180 mm Hg at presentation</td>
<td>No administration of nifedipine within 24 h without concomitant use of a β-blocker, and no administration of calcium channel blockers to patients with known LV dysfunction of at least moderate severity (LVEF &lt;0.40) or pulmonary edema at presentation</td>
</tr>
<tr>
<td>Appropriate recommendation for cardiac catheterization (A)</td>
<td>All with ≥1 high-risk feature as defined by the guideline, except those with cardiac catheterization within previous month, or those with increased risk for catheterization as defined by the guideline</td>
<td>Documentation of a physician’s recommendation for cardiac catheterization</td>
</tr>
<tr>
<td>Appropriate recommendation for coronary artery bypass surgery (A)</td>
<td>Any who underwent catheterization during the admission and were found to have significant 3-vessel or left main coronary disease, except those with severe distal disease of the native vessels or excessive risk for surgery as defined by the guideline</td>
<td>Documentation of physician’s recommendation for bypass surgery</td>
</tr>
<tr>
<td>Discharge aspirin therapy (A/B)</td>
<td>All except those with aspirin allergy, active bleeding, or high risk for bleeding, as defined by the guideline</td>
<td>Aspirin prescribed at discharge</td>
</tr>
</tbody>
</table>

* Grade A indicates evidence based on randomized controlled trials; grade B, primary evidence based on well-designed clinical studies; grade C, primary evidence was panel consensus; ECG, electrocardiography; LV, left ventricular; CHF, congestive heart failure; and EF, ejection fraction.

thrombolytic recommendation). A total of 189 patients (69%) had concordance scores of at least 80% (guideline-concordant care), and 112 (41%) had concordance scores of at least 69% (guideline-discordant care). A total of 189 patients had concordant care, and 112 (41%) had concordance scores of at least 80% (guideline-concordant care). A total of 189 patients had concordant care, and 112 (41%) had concordance scores of at least 80% (guideline-concordant care). A total of 189 patients had concordant care, and 112 (41%) had concordance scores of at least 80% (guideline-concordant care).

ONE-YEAR OUTCOMES AND OVERALL GUIDELINE CONCORDANCE

Kaplan-Meier survival curves (Figure 1) demonstrated improved survival for patients whose overall care was concordant with the guideline recommendations (log-rank P <.001 for survival and for survival free of myocardial infarction). In a univariate Cox analysis, guideline-discordant care was strongly associated with increased risk of postdischarge 1-year mortality (hazard ratio [HR], 4.3; 95% confidence interval [CI], 1.9-9.7; P <.001). Similarly, guideline-discordant care also predicted postdischarge death plus myocardial infarction by 1 year (HR, 3.2; 95% CI, 1.6-6.3; P <.001). Other univariate predictors of 1-year mortality and death plus myocardial infarction included increasing age, previous congestive heart failure, congestive heart failure at presentation, modified Charlson comorbidity index of 2 or greater, and elevated levels of creatinine at admission. Previous myocardial infarction was modestly associated with poorer survival (but not death plus myocardial infarction), whereas sex did not appear to be an important factor in either outcome. Similar results were obtained when the 5 patients who died in-hospital (2 with guideline-concordant and 3 with guideline-discordant care) were included in the analyses.

Table 2. Baseline Patient Characteristics°

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Guideline-Concordant Group (n = 189)</th>
<th>Guideline-Discordant Group (n = 86)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, y</td>
<td>64</td>
<td>70</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Male sex</td>
<td>70</td>
<td>62</td>
<td>.21</td>
</tr>
<tr>
<td>White race</td>
<td>92</td>
<td>90</td>
<td>.50</td>
</tr>
<tr>
<td>Rest angina</td>
<td>76</td>
<td>79</td>
<td>.54</td>
</tr>
<tr>
<td>Typical anginal symptoms</td>
<td>71</td>
<td>59</td>
<td>.07</td>
</tr>
<tr>
<td>Previous MI</td>
<td>45</td>
<td>56</td>
<td>.12</td>
</tr>
<tr>
<td>Previous revascularization</td>
<td>39</td>
<td>38</td>
<td>.89</td>
</tr>
<tr>
<td>Previous CHF</td>
<td>20</td>
<td>43</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Current smoker</td>
<td>24</td>
<td>16</td>
<td>.16</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>59</td>
<td>49</td>
<td>.15</td>
</tr>
<tr>
<td>CHF at presentation</td>
<td>23</td>
<td>51</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Charlson score ≥2</td>
<td>45</td>
<td>65</td>
<td>.004</td>
</tr>
<tr>
<td>Serum creatinine &gt;133 µmol/L</td>
<td>12</td>
<td>29</td>
<td>.001</td>
</tr>
<tr>
<td>(&gt;1.5 mg/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICU admission</td>
<td>29</td>
<td>17</td>
<td>.05</td>
</tr>
<tr>
<td>MI confirmed by enzymes</td>
<td>26</td>
<td>19</td>
<td>.22</td>
</tr>
</tbody>
</table>

* MI indicates myocardial infarction; CHF, congestive heart failure, and ICU, intensive care unit. Unless otherwise indicated, data are given as percentage of patients.
† Previous total cholesterol level of greater than 6.2 mmol/L (240 mg/dL) or receiving lipid-lowering therapy.

ONE-YEAR OUTCOMES AND INDIVIDUAL GUIDELINE RECOMMENDATIONS

Table 3 shows the 1-year Kaplan-Meier survival estimates for the 8 guideline recommendations considered separately. Survival in patients whose care was concor-
dant with the guideline was improved for each of the recommendations, although most of the differences in survival did not achieve statistical significance. One-year survival was nearly identical for patients who were referred for angiography according to guideline recommendations compared with patients who were not referred (88% vs 87%; $P = .91$). Thus, referral for angiography did not have a significant impact on outcome in this cohort of patients.

**BIVARIATE ANALYSES**

The impact of guideline-concordant care in patients of at least 65 years of age and in those with congestive heart failure was more thoroughly investigated by examining survival curves of the various subgroups (Figure 2). Again, guideline-concordant care was associated with improved survival in all subgroups, and the high-risk subgroups (aged $\geq 65$ years or with congestive heart failure at presentation) appeared to receive more benefit from guideline-concordant care compared with lower-risk subgroups.

**OUTCOMES WITH 100% CONCORDANCE**

The postdischarge 1-year survival of the 112 patients with a concordance score of 100% was 96%, compared with 87% in the 163 patients who had a score of less than 100% (log-rank $P = .008$). For postdischarge 1-year survival free of myocardial infarction, these figures were 91% and 82% (log-rank $P = .03$).

**COMMENT**

We have extended our evaluation of the AHCPR unstable angina guideline\(^1\) to investigate the association of guideline recommendations with 1-year clinical outcomes. Overall care concordant with 8 key guideline recommendations in this unselected cohort of patients with primary unstable angina was associated with approximately 4-fold reductions in risk for 1-year mortality and 3-fold reductions in risk for death or myocardial infarction. Further, care concordant with guideline recommendations was associated with improved survival for each of the 8 guideline recommendations, although not all associ-
ciations with each individual guideline were statistically significant. Of note, the survival advantage was greater for relatively simple recommendations that were unlikely to be affected by patient preference (eg, appropriate administration of aspirin, calcium channel blockers, or heparin), compared with more complex recommendations regarding the use of invasive procedures that may be more dependent on physician and patient preference.

Improved outcomes in patients receiving guideline-concordant care were particularly striking in higher-risk subgroups, such as patients at least 65 years of age or patients who present with unstable angina and congestive heart failure. Patients at least 65 years of age or with congestive heart failure who received guideline-discordant care had the poorest 1-year outcomes of any subgroup, whereas those who received guideline-concordant care had similar outcomes to lower-risk subgroups. Although there were improved outcomes seen in elderly patients and patients with congestive heart failure who received guideline-concordant care, these patients are in fact the least likely to receive guideline-concordant care, suggesting that future guidelines should focus further attention on these 2 high-risk subgroups. Our results regarding the benefits of appropriate treatment highlight the need for improved awareness among clinicians of the applicability of treatment recommendations to a broader range of patients with unstable angina.

VALIDATION OF PRACTICE GUIDELINE APPROACH

These results validate the approach adopted by the authors of the Unstable Angina guideline and, in a broader sense, provide support for the role of evidence-based medicine in clinical care. By basing their strongest recommendations on data from randomized controlled trials of treatment interventions,1 the authors of the guideline implicitly generalize the clinical trial results to a wider range of unselected patients with unstable angina. We used a simple method of guideline evaluation with easily obtained clinical information from a consecutive series of patients with unstable angina. Our method may be useful for policy makers, clinicians, and health care administrators to evaluate the quality of care in diverse hospital settings. For example, it would be of interest to evaluate the recently published recommendations of the American College of Chest Physicians12 and the current unstable angina guideline under development by the American College of Cardiology and the American Heart Association13 using similar methods to assess the applicability of these guidelines and their association with clinical outcomes. Our findings with the AHCPR guidelines support the hypothesis that individual recommendations and aggregate care can improve patient outcomes in the long term. The optimal design for testing this hypothesis may be a trial in which patients are randomized to compare fully guideline-concordant vs usual care.

Our observation that 1-year survival was nearly identical among patients with high-risk features who underwent catheterization as recommended in the guideline compared with those who did not is intriguing. Published randomized trial data to date do not demonstrate improved survival in patients with unstable angina who undergo routine early angiography. Although the guideline recommendation was based on the outcomes of the Thrombolysis in Myocardial Infarction (TIMI) IIIB trial that demonstrated equal early and late outcomes in the early-invasive and early-conservative treatment groups, the actual guideline recommendation is in fact more aggressive than the conservative treatment arm of TIMI IIIB. Although patients in the conservative arm of TIMI IIIB underwent angiography only if there was a failure of medical therapy, the guideline advises catheterization for a broader group that includes patients with high-risk features such as any previous revascularization, any previous left ventricular dysfunction (ejection fraction, <0.50), or the presence of congestive heart failure at presentation. The optimal angiography strategy for patients with unstable angina or non–Q-wave myocardial infarction remains elusive, with 2 recent trials demonstrating contradictory results (Veterans Affairs Non–Q-Wave Infarction Strategies in Hospital14 and FRAgmin and Fast Revascularisation during InStability in Coronary artery disease [FRISC II]15), and a third trial recently completed but not yet reported.16

POTENTIAL LIMITATIONS

We performed our retrospective review of patients with unstable angina at a single academic center, which may limit the generalizability of the results. We attempted to minimize information bias by selecting guideline recommendations that could be assessed reliably, using multiple sources for data abstraction and using standardized definitions applied by trained physician abstractors. Although the 8 recommendations we selected to evaluate represent only a portion of the 95 recommendations in the guideline, we attempted to identify those recommendations that were most clinically relevant and most strongly supported by an evidence-based approach (ie, grade A evidence based on randomized clinical trial data). The 3 remaining grade A recommendations not analyzed herein were purely descriptive or offered therapeutic options with regard to invasive vs conservative management, an issue that was addressed already to a large extent in the present analyses of the use of catheterization and bypass surgery.

It is also possible that unequal distribution of confounding factors other than guideline-concordant care was responsible in part for the observed differences in outcomes, and this possibility was addressed in 2 ways. First, we applied definitions of eligibility for each recommendation by the use of specific criteria detailed within the guideline (Table 1) in an attempt to identify ideal candidates for each guideline recommendation, and thus, further multivariate adjustment based on these criteria is not required. Second, we adjusted for noncardiac comorbidity by the use of a modified Charlson comorbidity index with diagnoses obtained from review of the medical record. Use of the medical record to calculate the Charlson comorbidity index has been shown to be superior to use of data obtained from the administrative billing record.17 Nonetheless, potential imbalances of confounding factors would be best addressed by a randomized clinical trial approach.
Last, the relatively small number of patients and clinical events increases the potential for type II errors and limits our ability to investigate potential confounders in multivariate modeling. However, the consistency of our findings across recommendations and subgroups supports our conclusion of improved outcomes with guideline-concordant care.

CONCLUSIONS

Patients treated according to the AHCPR unstable angina guideline experienced improved survival and survival free of myocardial infarction at 1 year. Improved outcomes were more marked in subgroups of patients at higher risk and were most evident for recommendations that were firmly based on randomized clinical trial data. These findings support the use of an evidence-based approach to guideline development and assessment of quality of care in patients with unstable angina.

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REFERENCES