

Relationship Between Glycosylated Hemoglobin Assessment and Glucose Therapy Intensification in Patients With Diabetes Hospitalized for Acute Myocardial Infarction

JOSHUA M. STOLKER, MD¹
 JOHN A. SPERTUS, MD, MPH²
 DARREN K. MCGUIRE, MD, MHSC³
 MARCUS LIND, MD⁴
 FENGMING TANG, MS²
 PHILIP G. JONES, MS²

SILVIO E. INZUCCHI, MD⁵
 SAIF S. RATHORE, PHD, MPH⁵
 THOMAS M. MADDOX, MD, MSC^{6,7}
 FREDERICK A. MASOUDI, MD, MSPH⁷
 MIKHAIL KOSIBOROD, MD²

OBJECTIVE—To evaluate the relationship between A1C and glucose therapy intensification (GTI) in patients with diabetes mellitus (DM) hospitalized for acute myocardial infarction (AMI).

RESEARCH DESIGN AND METHODS—A1C was measured as part of routine care (clinical A1C) or in the core laboratory (laboratory A1C, results unavailable to clinicians). GTI predictors were identified using hierarchical Poisson regression.

RESULTS—Of 1,274 patients, 886 (70%) had clinical A1C and an additional 263 had laboratory A1C measured. Overall, A1C was <7% in 419 (37%), 7–9% in 415 (36%), and >9% in 315 patients (27%). GTI occurred in 31% of patients and was more frequent in those with clinical A1C both before (34 vs. 24%, $P < 0.001$) and after multivariable adjustment (relative risk 1.34 [95% CI 1.12–1.62] vs. no clinical A1C).

CONCLUSIONS—Long-term glucose control is poor in most AMI patients with DM, but only a minority of patients undergo GTI at discharge. Inpatient A1C assessment is strongly associated with intensification of glucose-lowering therapy.

Diabetes Care 35:991–993, 2012

Diabetes mellitus (DM) is present among 25–35% of patients hospitalized for acute myocardial infarction (AMI) and confers a poor prognosis (1–4). Although A1C assessment is recommended for patients with DM hospitalized for an acute illness (5), whether inpatient A1C assessment impacts DM management during AMI remains unclear. We studied patients with DM in a multicenter AMI registry to evaluate the frequency of A1C assessment and its relationship with glucose therapy intensification (GTI) at discharge.

RESEARCH DESIGN AND METHODS

Patient population

The Translational Research Investigating Underlying Disparities in Acute Myocardial Infarction Patients' Health Status (TRIUMPH) study is a prospective AMI registry at 24 U.S. hospitals (6). In this analysis, patients with known DM (self-reported or documented in the chart) or those on glucose-lowering drugs on admission were included.

Data definitions

Patients were considered to have clinical A1C if measured during hospitalization or obtained in the preceding 3 months. Patients consenting to TRIUMPH laboratory assessments also had A1C measured separately (laboratory A1C); these results were not available to treating clinicians. Standard A1C cut points were used (good, suboptimal, and poor control for A1C <7, 7–9, and >9%, respectively) (7). GTI was defined as increase in the dose of an oral antihyperglycemic agent, addition of a new antihyperglycemic agent, or $\geq 20\%$ increase in daily insulin dose on discharge versus admission (8). Changing one oral agent to another was not considered GTI.

Statistical approach

Hierarchical Poisson regression models (controlling for clustering by hospital) were constructed to identify independent predictors of GTI. Candidate variables included demographics, factors associated with GTI in bivariate analysis, or those considered a priori as clinically important (BMI, admission glucose, mean fasting glucose, clinical A1C, intravenous insulin infusion, and admission DM medications). To evaluate whether physicians are more likely to prescribe GTI in patients with worse glycemic control when A1C is clinically available (versus when A1C levels are not known), we performed a secondary analysis in which GTI rates were compared between patients with clinical A1C versus laboratory A1C only within each glucose control subgroup (good, suboptimal, and poor).

RESULTS

A1C assessment

Between 2005 and 2008, TRIUMPH enrolled 1,274 AMI patients with DM on admission (6% type 1, 87% type 2, and 7% unknown type). Clinical A1C assessment was performed in 886 patients (70%), and an additional 263 individuals

From ¹Saint Louis University, St. Louis, Missouri; ²Saint Luke's Mid America Heart and Vascular Institute, Kansas City, Missouri; the ³University of Texas Southwestern Medical Center, Dallas, Texas; the ⁴University of Gothenburg, Gothenburg, Sweden; ⁵Yale University, New Haven, Connecticut; the ⁶VA Eastern Colorado Health Care System, Denver, Colorado; and the ⁷University of Colorado Denver, Denver, Colorado.

Corresponding author: Joshua M. Stolker, jstolker@yahoo.com.

Received 22 September 2011 and accepted 16 January 2012.

DOI: 10.2337/dc11-1839

© 2012 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. See <http://creativecommons.org/licenses/by-nc-nd/3.0/> for details.

had laboratory A1C measured. Of these 1,149 patients with known A1C levels, glycemic control was good in 419 (37%), suboptimal in 415 (36%), and poor in 315 patients (27%).

Rates and predictors of GTI

Overall, 396 of 1,274 patients (31%) had GTI at hospital discharge (33% new oral medication, 37% new insulin, 5% new oral medication and insulin, 9% oral medication up-titration, and 15% insulin increase). GTI was more frequent in patients with versus without clinical A1C assessment (34 vs. 24%, $P < 0.001$). In patients with clinical A1C, GTI rates increased with progressively worse glucose control (16, 37, and 55% with A1C levels <7 , 7–9, and $>9\%$, respectively; $P < 0.001$). Moreover, physicians were more likely to prescribe GTI in patients with suboptimal or poor glucose control when A1C was clinically available (Fig. 1).

Independent predictors of GTI included clinical factors (higher BMI, lack of insurance, no insulin before AMI, and fewer DM medications before AMI) and several glucose-related factors: presence of clinical A1C (relative risk 1.34 [95% CI 1.12–1.62]), higher A1C (1.86 [1.40–2.45] for A1C 7–9% and 2.45 [1.63–3.67] for A1C $>9\%$, vs. A1C $<7\%$), and higher fasting glucose during hospitalization (1.19 [1.10–1.29] per one SD increase [52 mg/dL]). After multivariable adjustment, presence of clinical A1C was independently associated with higher GTI rates in each glucose control subgroup, versus patients with laboratory

A1C only (1.30 [1.06–1.59] for A1C $<7\%$, 2.14 [1.13–4.04] for A1C 7–9%, and 1.78 [1.06–2.97] for A1C $>9\%$; interaction $P = 0.30$).

CONCLUSIONS—Although guidelines recommend A1C assessment for all hospitalized patients with DM (if not recently measured) (5), we found that only 70% of AMI patients with DM had A1C levels measured clinically. When assessed, nearly two-thirds of patients with DM had suboptimal or poor long-term glycemic control, but only a minority underwent intensification of their glucose-lowering therapy by hospital discharge. Of note, clinical A1C assessment was strongly and independently associated with GTI during AMI hospitalization, especially in patients with suboptimal and poor glucose control.

Clinical implications

Although this analysis shows modest improvement in A1C assessment compared with earlier data (8), nearly one in three patients with DM still do not have A1C checked during AMI hospitalization. The observed association between clinical A1C availability and higher rates of both GTI and nonpharmacologic measures (8) in patients with suboptimal and poor glucose control suggests that presence of clinical A1C may lead to important therapeutic interventions for DM management. In addition, many physicians relegate DM evaluation to the outpatient setting, but chronic DM management is not consistently addressed after hospital discharge

post-AMI (8,9). Although randomized trials have not demonstrated reductions in cardiovascular events with intensive glucose control (10,11), better glucose control does reduce microvascular complications of DM, and optimization of A1C levels continues to be recommended by professional societies (5,12). Incorporating routine A1C assessment as part of in-hospital care for AMI patients with DM represents an opportunity to emphasize individualized, patient-centered DM management during AMI hospitalization that may improve transition to the outpatient setting, and potentially reduce long-term DM-related complications.

Limitations

Only patients with established DM and AMI were included in this study, so its implications cannot be extrapolated to patients with prediabetic states or newly diagnosed DM, and generalizability of findings to other hospitalized patients is unknown. Information about GTI during the immediate postdischarge period was not available, and some patients may have received GTI during early outpatient follow-up. Furthermore, the impact of therapeutic intensification on clinical outcomes remains unclear, as our study was not designed to address this question.

Summary

Nearly two-thirds of hospitalized AMI patients with DM have suboptimal or poor long-term glycemic control, but only a minority receives intensification of glucose-lowering therapy at discharge. Inpatient A1C assessment is strongly associated with higher rates of GTI, particularly when glycemic control is suboptimal or poor. Future studies should evaluate whether clinical outcomes are affected by intensification of glucose-lowering therapy after AMI in patients with poor glucose control.

Acknowledgments—Funding for this analysis was provided by a grant from sanofi-aventis. J.M.S. has served on the speaker's bureau for AstraZeneca. J.A.S. received research grant support from sanofi-aventis, Bristol-Myers Squibb, Eli Lilly, and Amgen. D.K.M. served as a consultant to Tethys Biosciences, Novo Nordisk, F. Hoffman LaRoche, Genentech, sanofi-aventis, Pfizer, Boehringer Ingelheim, and Daiichi Sankyo. M.L. received research grant support from AstraZeneca, Novo Nordisk Scandinavia, and Abbott Scandinavia; served on an advisory board for Novo Nordisk

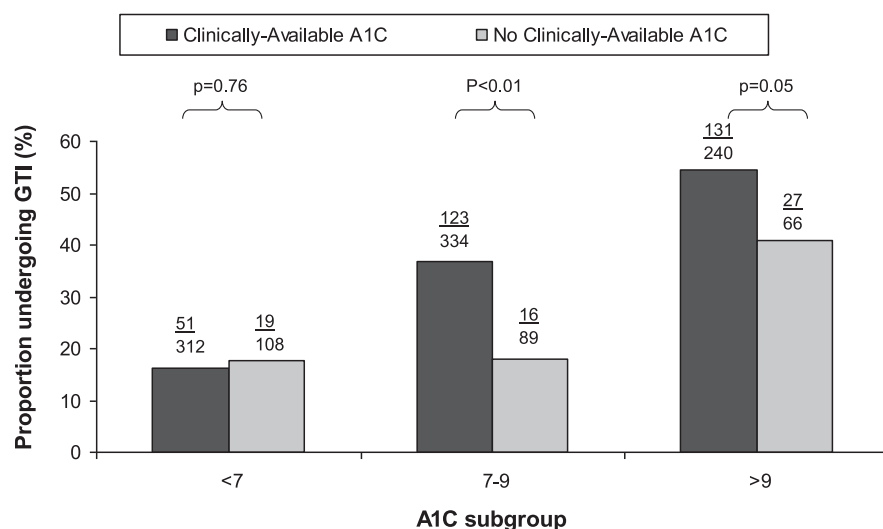


Figure 1—GTI stratified by subgroup of glycemic control. A1C indicates glycosylated hemoglobin.

Scandinavia; and served as a consultant to Eli Lilly, Medtronic, Novartis, Novo Nordisk Scandinavia, Pfizer, and sanofi-aventis. S.E.I. received research grant support from Eli Lilly; served as a consultant to Takeda, Merck, and Boehringer Ingelheim; and received speaking honoraria from Novo Nordisk. F.A.M. received grant support from Amgen and has been a member of the advisory board for Takeda Pharmaceuticals. M.K. served as a consultant for sanofi-aventis, Boehringer Ingelheim, Gilead, Kowa Pharmaceuticals, Genentech, and Medtronic Diabetes and has research grant support from Medtronic Diabetes. No other potential conflicts of interest relevant to this article were reported.

sanofi-aventis had no role in the design of this study, statistical analysis, or approval of the manuscript.

J.M.S. and M.K. conceived and designed the study and wrote the manuscript. J.A.S. and D.K.M. provided critical recommendations regarding study design and methodology, critically reviewed the manuscript, and provided editorial recommendations. M.L., S.E.I., S.S.R., T.M.M., and F.A.M. critically reviewed the manuscript and provided editorial recommendations. F.T. and P.G.J. performed statistical analyses. J.M.S. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

This study was presented previously in abstract form at the 45th European Association for the Study of Diabetes Annual Meeting, Vienna, Austria, 27 September–1 October 2009;

the American Heart Association (AHA) 2009 Scientific Sessions, Orlando, Florida, 14–18 November 2009; and the AHA Quality of Care and Outcomes Research in Cardiovascular Disease and Stroke 2010 Scientific Sessions, Washington, DC, 19–21 May 2010.

References

1. Donahoe SM, Stewart GC, McCabe CH, et al. Diabetes and mortality following acute coronary syndromes. *JAMA* 2007; 298:765–775
2. Mak KH, Moliterno DJ, Granger CB, et al. Influence of diabetes mellitus on clinical outcome in the thrombolytic era of acute myocardial infarction. *J Am Coll Cardiol* 1997;30:171–179
3. Abbott RD, Donahue RP, Kannel WB, Wilson PW. The impact of diabetes on survival following myocardial infarction in men vs. women. The Framingham Study. *JAMA* 1988;260:3456–3460
4. Norhammar A, Lindbäck J, Rydén L, Wallentin L, Stenstrand U; Register of Information and Knowledge about Swedish Heart Intensive Care Admission (RIKS-HIA). Improved but still high short- and long-term mortality rates after myocardial infarction in patients with diabetes mellitus: a time-trend report from the Swedish Register of Information and knowledge about Swedish heart intensive care admission. *Heart* 2007;93:1577–1583
5. American Diabetes Association. Standards of medical care in diabetes—2011. *Diabetes Care* 2011;34(Suppl. 1):S11–S61
6. Arnold SV, Chan PS, Jones PG, et al.; Cardiovascular Outcomes Research Consortium. Translational research investigating underlying disparities in acute myocardial infarction patients' health status (TRIUMPH): design and rationale of a prospective multicenter registry. *Circ Cardiovasc Qual Outcomes* 2011;4:467–476
7. American Diabetes Association. Standards of medical care in diabetes—2010. *Diabetes Care* 2010;33(Suppl. 1):S11–S61
8. Stolker JM, Sun D, Conaway DG, et al. Importance of measuring glycosylated hemoglobin in patients with myocardial infarction and known diabetes mellitus. *Am J Cardiol* 2010;105:1090–1094
9. Barnes CS, Ziemer DC, Miller CD, et al. Little time for diabetes management in the primary care setting. *Diabetes Educ* 2004; 30:126–135
10. Gerstein HC, Miller ME, Byington RP, et al.; Action to Control Cardiovascular Risk in Diabetes Study Group. Effects of intensive glucose lowering in type 2 diabetes. *N Engl J Med* 2008;358:2545–2559
11. Patel A, MacMahon S, Chalmers J, et al.; ADVANCE Collaborative Group. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. *N Engl J Med* 2008;358:2560–2572
12. Czupryniak L. Guidelines for the management of type 2 diabetes: is ADA and EASD consensus more clinically relevant than the IDF recommendations? *Diabetes Res Clin Pract* 2009;86(Suppl. 1):S22–S25