Relationship Between Care Gaps and Projected Life Expectancy After Acute Myocardial Infarction

Dennis T. Ko, MD, MSc; Peter C. Austin, PhD; Jack V. Tu, MD, PhD; Douglas S. Lee, MD, PhD; Lingsong Yun, MSc; David A. Alter, MD, PhD

Background—Higher-risk patients may not receive evidence-based therapy because of limited life expectancy, which is a composite measure that encompasses many patient factors, including age, frailty, and comorbidities. In this study, we evaluated the extent to which treatment care gaps can be explained by a difference in projected life expectancy.

Methods and Results—An observational cohort study was conducted on acute myocardial infarction patients hospitalized in Ontario, Canada. Projected life expectancy was estimated using actual survival data with extrapolation using proportional hazard models adjusting for important covariates. The relationship between projected life expectancy with statins and reperfusion therapy was examined using generalized linear models. Among the 7001 acute myocardial infarction patients, 84.3% were prescribed statins and 72.9% were treated with reperfusion therapy. When projected life expectancy was <10 years, the likelihood of receiving either treatment declined progressively with reduction in life expectancy (P<0.001). At the 25th percentile of projected life expectancies, the likelihood of receiving a statin decreased by 1.4% (95% confidence interval, 1.0–1.8%), and acute reperfusion therapy decreased by 2.6% (95% confidence interval, 1.8–3.3%) for each year decline in projected life expectancy.

Conclusions—Life expectancy of a patient strongly influences evidence-based treatment in acute myocardial infarction. It was seen not only among patients with limited life expectancies but also among those with many years to live. Treatment care gaps may reflect clinicians’ synthesis about frailty and life-expectancy gains. (Circ Cardiovasc Qual Outcomes. 2014;7:581-588.)

Key Words: health services research ■ life expectancy ■ myocardial infarction
WHAT IS KNOWN

- Evidence-based therapies for treating acute myocardial infarction are underutilized and accordingly, opportunities to improve patient outcomes may be lost.

WHAT THE STUDY ADDS

- Through the comprehensive analysis of a large population-based acute myocardial infarction data set, we found that life expectancy of a patient strongly influences evidence-based treatment in acute myocardial infarction.
- The relationship between life expectancy and treatment was seen not only among patients with limited life expectancies, but also among those with many years to live.
- The results of this study suggest that treatment care gaps may reflect clinicians’ synthesis about frailty and life-expectancy gains.

Survival prediction model avoids the use of parametric assumptions and incorporates empirical patient-level data to extrapolate survival beyond an observed follow-up period, and estimates the hazards of death as a function of age (as opposed to time) to allow for the estimation survival distribution of the entire population. This age-based adjusted survival prediction model avoids the use of parametric assumptions or simulation techniques. It has been evaluated against traditional survival analytic techniques, and applied to clinical trial data, observational studies, and cost-effectiveness analyses.5–12

In our study, we estimated the life expectancy for each myocardial infarction patient who survived to hospital discharge with the following steps. First, the observed 2-year survival in the EFFECT cohort was modeled using a traditional time-based Cox proportional hazards model with time-to-death as the primary outcome. The model adjusted for age, sex, and variables that were previously found to be important predictors of adverse outcomes in the Global Registry of Acute Coronary Events (GRACE) study including admission characteristics (heart rate, Killip class, systolic blood pressure, cardiac arrest at admission, ST-segment deviation), and laboratory values (serum creatinine, positive cardiac markers).13 The GRACE model had been previously validated by our group to have good predictive ability in the EFFECT cohort.14 In addition, although it was originally developed to predict short-term outcomes, it has also been demonstrated to predict long-term mortality accurately.15 A traditional Cox model was used because the hazard of death after myocardial infarction hospitalization varies significantly in the initial months, violating the assumption of the age-based model that depends on hazard rate remaining stable over time.

Second, among patients surviving to 2 years and beyond, we used an age-based Cox proportional hazard model to generate age-specific predicted survival curves. This model used left-truncated and right-censored data (subjects entered follow-up at a given age and were followed up to age of death or age at time of censoring). The age-based hazard of death was modeled as a function of baseline covariates as previously described. A survival curve was estimated for each subject from a fitted survival model as a function of patient age (from age at 2 years postindex date onwards). This allowed us to determine survival conditional on a patient surviving to after the index date. Age-specific survival curves (conditional on patients surviving the first 2 years) were then concatenated to time-specific survival curves (i.e., the probability of surviving for the number of additional years) for each patient based on the covariates pattern. Third, the survival probabilities derived from the 2 steps were combined to estimate the expected life expectancy of each myocardial infarction patient.

Treatment of Interest

We examined 2 therapies as test cases to gain insights into the relationship between life expectancy and treatment propensity, because we hypothesized that the impact of projected life expectancy may differ between acute and chronic therapy. We chose statin therapy at hospital discharge for patients with myocardial infarction and acute reperfusion therapy (fibrinolytic or primary percutaneous coronary intervention) for patients with ST-segment–elevation myocardial infarction within 12 hours of symptom onset. We excluded patients who had a history of dementia, metastatic cancer, end-stage renal failure on hemodialysis, and patients with a do-not-resuscitate order in all our analyses (Table 1 in the Data Supplement). Our goal was to construct a cohort that resembled clinical trial inclusion criteria where even higher-risk patients would be suitable and potentially derive benefit from therapy.

Statistical Analysis

Baseline characteristics of patients who received each treatment of interest were compared with patients who did not receive treatment using 2 tests for categorical variables and Wilcoxon Rank Sum test for continuous variables. We then explored the relationship between receipt of treatment and life expectancy by dividing the patient cohort into 50 mutually exclusive strata, each comprising 2% of the study sample, using the 50 quantiles of the distribution of life expectancy. After calculating projected life expectancy and treatment utilization in each of the 50 strata, we regressed utilization rate of treatment on mean life expectancy and its higher functions (quadratic and cubic), using a generalized linear model with a gamma distribution and with a logarithmic link function. Predicted utilization rates were estimated using this model at different percentiles of the projected life expectancy.
expectancy, which allowed us to (a) calculate the average change of treatment utilization per each year of change in life expectancy and (b) examine this relationship qualitatively by plotting predicted prescribed rates of statins and reperfusion therapy use versus projected life expectancy.

Additional analyses were performed to delineate the relationship between age and life expectancy and to evaluate whether the association of life expectancy with treatment was due to the effect of age alone. First, we examined the relationship between age and projected life expectancy for each myocardial infarction patient in...
our cohort, graphically using a scatter plot. Second, we examined the prescription of statins and utilization reperfusion therapy with age, in different strata based on the estimated life expectancy of a patient (<10 years, 10–15 years, and >15 years). Finally, we examined the prescription of statins and utilization reperfusion therapy with life expectancy, in different strata based on age of the patient (50–75 years, >75 years).

A series of additional analyses were conducted to examine the robustness of our results. First, we performed an additional analysis examining the relationship between treatment and projected life expectancy, using the 5-year survival data in the EFFECT cohort (instead of 2 years) to estimate life expectancy of myocardial infarction. Second, we examined the relationship between treatment and life expectancy in the eligible candidates (instead of ideal candidates). These analyses demonstrated similar relationship of either treatment with projected life expectancy as our original analyses.

We conducted the statistical analyses using the SAS version 9.2 (SAS Institute, Inc, Cary, NC) software. This study was approved by Sunnybrook Health Sciences Center’s Research Ethics Board. \(P\) values were generated from the models. All statistical tests were 2-tailed and \(P\) values of <0.05 were considered statistically significant.

### Results

#### Baseline Characteristics

The EFFECT cohort included 7889 hospitalized myocardial infarction patients. After excluding patients with dementia, metastatic cancer, and end-stage renal disease, and patients with a do-not-resuscitate order, our study sample consisted of 7001 AMI patients. The mean age of the study cohort was 67.6 years, 35.2% were women, and 27.1% had a history of diabetes mellitus. One-year mortality was 17.1% and the estimated mean life expectancy was 12.4 years.

Among ideal candidates, the prescription rate was 84.3% for statin therapy at hospital discharge and the utilization rate was 72.9% for acute reperfusion therapy for patients with ST-segment–elevation myocardial infarction. The demographic and clinical characteristics of patients who received statins and acute reperfusion therapy differed significantly from those of patients who did not (Table 1). In general,
patients who received treatments were younger, more likely to be men, had fewer comorbidities, and a higher estimated life expectancy. As shown in Figure I in the Data Supplement, there was significant variation in the estimated life expectancy for similarly aged patients. For example, the life expectancy of a 70-year-old myocardial infarction patient ranged from 1.5 to 14 years.

**Relationship Between Treatments and Life Expectancy**

Figures 1 and 2 illustrate the relationship between statin use and acute reperfusion therapy with projected life expectancies. A significant relationship between treatment and life expectancy was observed for both therapies ($P<0.001$). In addition, the relationship seemed nonlinear. For patients who had projected life expectancies of <10 years, the likelihood of receiving evidence-based therapies progressively declined with decreasing life expectancies. For patients who had projected life expectancies of >10 years, the likelihood of receiving evidence-based therapies remained relatively constant with changes in projected life expectancies.

The estimated change in treatment utilization according to the projected life expectancy decile is shown in Table 2. At the 25th percentile of projected life expectancies, the likelihood of receiving a statin was decreased by 1.4% (95% confidence interval, 1.0–1.8%), and of undergoing acute reperfusion by 2.6% (95% confidence interval, 1.8–3.3%) for each year decline in projected life expectancy (Table 2).

An additional analysis was performed among eligible patients for therapy (instead of ideal candidates), which showed a similar relationship between prescription of statins and acute reperfusion therapy with projected life expectancy.

**Relationship Between Treatments and Life Expectancy in Different Subgroups**

To delineate the impact of age and life expectancy on the propensity of treatment, we further evaluated the relationship by stratifying the cohort based on prespecified estimated life expectancy groups. We observed a significant and progressive decline in the use of both therapies with increasing age when the estimated life expectancy was <10 years. No significant correlation between age and treatment was observed for patients with estimated life expectancy >10 years (Figures 3 and 4). We also evaluated the relationship between treatment and life expectancy in different age groups. We observed a significant and progressive decline in the use of both therapies with decreasing life expectancy even in the younger age group of 50 to 75 years (Figures II and III in the Data Supplement).
Discussion

Our study extends prior findings on treatment gaps of AMI by evaluating a global measure of projected life expectancy. Using a population-based cohort of patients who survived myocardial infarction, we demonstrated that the projected life expectancy of a patient strongly influences treatment utilization. First, we observed a progressive decline in the use of therapy with decreasing life expectancies. Second, this relationship was consistent across our test cases, which included chronic therapy (statins) and acute therapy (reperfusion). Lastly, the association between treatment and life expectancies was seen not only among patients with limited prognosis but also among those who were expected to live for 10 to 15 years. Our findings suggest that the persistent treatment care gaps may reflect clinicians' synthesis about frailty and life-expectancy gains, which could be minimized only with a better understanding of the prognosis of older patients with comorbidities.

To the best of our knowledge, this is the first study to elucidate the importance of projected life expectancy and treatment propensity. We think our findings match the clinical observation proposed by Spertus and Furman\textsuperscript{6} that many decisions are based on clinicians attempting to identify who might be too sick to warrant the hassle of more complex medical or invasive regimens at the bedside. Our methodology of measuring life-expectancy is an improvement when compared with the traditional life table method because it allows estimation of average life expectancy accurately in cohorts where not all deaths have occurred. Prognostication using life-expectancy can theoretically play an important role in clinical decision-making particularly among high-risk patients or individuals near their end-of-life. For example, eligibility for hospice care usually requires that patients have a life expectancy of <6 months.\textsuperscript{16} Similarly, current guidelines recommend consideration of implantable cardioverter defibrillator or transcatheter aortic valve implantation for patients with a life expectancy of $\geq$ 1 year.\textsuperscript{17,18}

We initially hypothesized that the relationship between projected life expectancy and the receipt of therapies may have differed based on the duration within which therapeutic responsiveness was expected to emerge. For example, the decision to use chronic therapies such as statins may be governed by the expectations that clinical benefits emerge over longer time-intervals, and accordingly, may be more influenced by the life expectancy of an individual than acute life-saving therapies whose benefits are more immediate. However, our results suggested that this was not the case. The relationship between projected life expectancies and treatment utilization was the same for both acute reperfusion therapy and chronic statin use, suggesting that treatment

![Figure 4](http://circoutcomes.ahajournals.org/)

Figure 4. The relationship between age and reperfusion therapy is shown in (A) life expectancy <10 years, (B) life expectancy 10 to 15 years, and (C) life expectancy >15 years.
decisions among otherwise eligible patients are governed by similar factors that may, as in the case of our study, correlate with life-expectancy. We did find a slightly greater reduction in the use of acute reperfusion therapy compared with statin prescription with declining life expectancy. For example, the likelihood of being prescribed a statin decreased by 1.6% versus 3.1% for receiving acute reperfusion therapy at the lowest 10th percentile of projected life expectancy. Prior study has suggested that the lower treatment propensity for higher risk patients is associated with clinicians’ concerns of patients experiencing adverse events with acute reperfusion therapy.  

To overcome this care gap, we think a paradigm shift in improving our understanding of life expectancies is needed. The primary issue is that the majority of current clinical prediction tools estimate baseline risks of patients. A better approach may be to provide an estimation of baseline risks coupled with treatment-related adverse rates, and provide an overall estimation of treatment benefits and estimated life-expectancy gains. Furthermore, we propose that randomized trials estimate treatment benefits not only in terms of relative and absolute reduction, but also to include gains in life expectancy. Although this may be challenging because most randomized trials have a relatively short follow-up period, linking trial data to administrative data with extended outcomes or using prediction models or both, as we have done in this study, is increasingly feasible.

Notwithstanding the importance of life expectancy when explaining care gaps, the care patterns observed in our study are likely inappropriate based on clinical trial evidence. Specifically, all patients examined in our study were deemed ideal candidates for each of their respective therapies. We excluded patients with potential contraindications to therapies similar to those in patients who have been evaluated in clinical trials. However, we also recognized that only a minority of patients included in clinical trials were elderly or had limited life expectancy.

Several potential limitations of our study merit discussion. First, our main intention was to explore the relationship between treatment gaps and projected life expectancies in a qualitative manner. Our study was not intended to evaluate threshold effect or the inflection point at which clinical practice changes based on the life expectancy of a patient. Second, we excluded patients with severe comorbidities (dementia, metastatic cancer, hemodialysis, do-not-resuscitate order) because these patients have historically not been included in clinical trials. Including these patients would tend to amplify the relationship we observed between treatment and projected life expectancy. Third, we did not include all the factors that may influence treatment decisions such as functional capacity, mental status change, unexplained weight loss, or other potentially important clinical factors. Furthermore, it is important to note that our cohort of AMI patients was assembled from 2004 to 2005, and treatment patterns may have changed over time. Finally, although the calculation of projected life expectancy was previously validated, we were unable to validate our estimates against the actual estimates in the EFFECT cohort because the majority of patients were still alive in our study cohort.

In conclusion, we demonstrated that evidence-based care gap disparities may be explained by the unequal provision of therapies according to the estimated life expectancies of patients. Although treatment related adverse events are likely higher in patients with a shorter life expectancy, this pattern of treatment avoidance is likely not justified because meaningful gains in life expectancy can still be expected in a majority of patients.

Sources of Funding

The analysis of this study was supported by a Canadian Institutes of Health Research (CIHR) operating grant MOP (102487). Dr Ko is supported by a Clinician Scientist Award from the Heart and Stroke Foundation of Canada, Ontario branch. Dr Tu is supported by a Canada Research Chair in Health Services Research and a Career Investigator Award from the Heart and Stroke Foundation of Ontario (HSFO). Dr Lee is supported by a CIHR Clinician Scientist Award. Dr Austin and Dr Alter are supported by a Career Investigator Award from the Institute for Clinical Evaluative Sciences (ICES), which is funded by an annual grant from the Ontario Ministry of Health and Long-Term Care (MOHLTC). The opinions, results, and conclusions reported in this article are ours and are independent of the funding sources. No endorsement by ICES or the Ontario MOHLTC is intended or should be inferred.

Disclosures

None.

References

5. Austin PC, Tu JV, Ko DT, Alter DA. Factors associated with the use of evidence-based therapies after discharge among elderly patients with myocardial infarction. CMAJ. 2008;179:901–908.

Ko et al Care Gaps and Life Expectancy 587


Relationship Between Care Gaps and Projected Life Expectancy After Acute Myocardial Infarction

Dennis T. Ko, Peter C. Austin, Jack V. Tu, Douglas S. Lee, Lingsong Yun and David A. Alter

Circ Cardiovasc Qual Outcomes. 2014;7:581-588; originally published online June 3, 2014;
doi: 10.1161/CIRCOUTCOMES.113.000795

Circulation: Cardiovascular Quality and Outcomes is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2014 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-7705. Online ISSN: 1941-7713

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circoutcomes.ahajournals.org/content/7/4/581

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Cardiovascular Quality and Outcomes can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at: http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Cardiovascular Quality and Outcomes is online at:
http://circoutcomes.ahajournals.org//subscriptions/