# Does Aggressive Care Following Acute Myocardial Infarction Reduce Mortality? Analysis with Instrumental Variables to Compare Effectiveness in Canadian and United States Patient Populations

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**Background.** Previous U.S. studies suggest that the incremental ("marginal") use of the aggressive approach to care for acute myocardial infarction (AMI) in patients differing only in their distance to hospitals offering aggressive care may be associated with small mortality benefits. We hypothesized that the marginal benefits should be larger in Canada, as the country is operating on a lower margin because the approach to care is more conservative overall.

**Methods.** This retrospective study used administrative data of hospital admissions and health services for all patients admitted for a first AMI in Quebec in 1988 ($n = 8{,}674$). We used differential distances to hospitals offering aggressive care as instrumental variables when measuring mortality up to four years after AMI.

**Results.** Of the 4,422 subjects who were ≥65 years old, 11 percent received cardiac catheterization within 90 days after admission. In a previous study that applied similar methodology to the 1987 U.S. Medicare population, 23 percent of subjects received catheterization within 90 days. As in the U.S. study, we found that subjects living closer to hospitals offering aggressive care were more likely to receive aggressive care than subjects living further away (26 percent versus 19 percent received cardiac catheterization within 90 days; 95 percent CI: 5 percent to 9 percent). Unlike the U.S. study, we found no differences in mortality across the "close" versus "far" differential distance groups (unadjusted differences at one year: 1 percent; 95 percent CI: −1 percent to 3 percent). This absence of association held in elderly (≥65 years) and younger age groups. Adjusted results also showed no differences between subjects receiving aggressive versus conservative care (at one year: 4 percent; 95 percent CI: −11 percent to 20 percent).

**Conclusions.** Contrary to our hypothesis, but consistent with results from numerous randomized trials and observational studies, we cannot confirm that, on the margin, the aggressive approach to post-AMI care is associated with mortality benefits in Canada.

**Key Words.** Myocardial infarction, instrumental variables, administrative database, confounding bias, mortality, Canada, United States

Most regions of the United States tend to adopt an aggressive approach to care for acute myocardial infarction (AMI)—using invasive procedures such as cardiac catheterization in all patients and revascularization in most patients—while most Canadian regions favor a conservative approach—using invasive procedures more selectively (Pilote, Racine, and Hlatky 1994; Pilote, Granger et al. 1995; Pilote et al. 1998; Pilote, Bourassa et al. 1995). Whether or not the aggressive approach reduces mortality in comparison to more conservative approaches remains a topic of intensive investigation (Tu et al. 1997). There is therefore increasing interest in using data from administrative sources to evaluate the effectiveness of AMI treatment approaches in "real-world" patient populations. However, one important limitation of administrative database research is a strong potential for confounding bias, due to differences between comparison groups in terms of patient characteristics that have not been captured in the database (Ray 1997; Byar 1991).

One approach that has been proposed to deal with this bias is the use of instrumental variables (Newhouse and McClellan 1998; Zohoori and Savitz 1997). In the instrumental variable estimation strategy, an instrumental variable is used in analyses to form groups of subjects that are unrelated to confounding variables, but that have different probabilities of receiving a particular treatment (Ho, Hamilton, and Roos 2000; Ettner, Hermann, and Tang 1999; Gowrisankaran and Town 1999). In this sense, instrumental variable estimation allows a pseudorandomization of study subjects. For this pseudorandomization to occur, the instrumental variable must be associated with the main independent variable but not be directly associated with the outcome variable of interest (Greenland 2000). The differences in care received across instrumental variable groups allows for unbiased estimation of the effects of a treatment for the "marginal" subpopulation of subjects whose type of care received was dependent on the instrumental variable (Harris and Remler 1998).

McClellan et al. used instrumental variable estimation to investigate whether the aggressive approach reduced mortality in marginal, elderly U.S. Medicare beneficiaries who were admitted for AMI in 1987 (McClellan, McNeil, and Newhouse 1994). This study confirmed the presence of

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appreciable bias in standard outcome measures due to unobserved differences between groups of subjects receiving aggressive or conservative care, and the likelihood of less bias in outcome measures following the application of the instrumental variable approach. Standard analytical methods indicated that there were large benefits from aggressive care, while outcome measures obtained using instrumental variable methodology showed only minimal benefits. Two later studies showed small, but statistically significant, mortality benefits using this methodology (McClellan 1996; Brooks, McClellan, and Wong 2000).

To more fully evaluate the usefulness of instrumental variable methodology, it is important that it be reapplied in different patient populations. In particular, it should be reapplied in populations from regions that adopt different approaches to post-AMI care, as the regions will be operating on different margins. In each region, there will be a group of patients that would clearly benefit from aggressive care, a group that would clearly not benefit, and a group for whom a benefit is possible but not clear. It is likely that the marginal patients are drawn from this latter group. As the approach to care becomes more aggressive overall within a region, the expected benefits for the marginal patients become smaller. Thus, we would expect the marginal mortality benefits resulting from aggressive care in regions with more conservative care (lower margin) to be greater than the marginal mortality benefits in regions with more aggressive care (higher margin). For instance, the marginal benefits of aggressive care should be greater in Canada than in the United States. Although there are striking regional differences in the rate of use of aggressive post-AMI care within the United States (Pilote, Racine, and Hlatky 1994; Pilote, Granger et al. 1995; Pilote et al. 1998; Pilote, Bourassa et al. 1995; Tu et al. 1997), the effect of these differences on the marginal benefit of such care has not been previously explored.

The main objective of this study was to evaluate the marginal effects of an aggressive approach to post-AMI care on mortality in a Canadian patient population. We used an administrative database of all patients sustaining a first AMI in Quebec in 1988. By obtaining data from this time period, and by using the analytic approach used by McClellan et al. (McClellan, McNeil, and Newhouse 1994), we were able to compare our results to those previously obtained for the U.S. Medicare population. Unlike the U.S. Medicare database, the Quebec database includes AMI patients of all ages and not only patients aged 65 years and older. Therefore, a secondary objective of this study was to compare the effects of more aggressive care in patients younger than 65 years old to the effects in older patients.

# METHODS

## *Subjects*

Data on the treatment and clinical outcomes of all patients who sustained a first AMI in Quebec in 1988 ($n = 8,995$) were obtained retrospectively from two government administrative databases: the Quebec hospital discharge summary database (Med-Echo), and the Quebec Medicare database (*la Régie de l'assurance maladie du Québec* [RAMQ]). The Med-Echo database was used to identify study patients with a main discharge diagnosis of AMI (ICD-9 code 410). The absence of a code for AMI was ascertained for at least three years preceding the diagnosis. The positive predictive value for coding an AMI for elderly survivors in this database has been evaluated to be 96 percent (95 percent CI: 94 percent to 98 percent) (Levy et al. 1999). Patient demographic and hospital characteristics were identified from these data. Secondary diagnoses were used to obtain data on subjects' comorbid diseases. Postal codes (first three digits) for the patients' residence at the time of their discharge were also identified for 99.4 percent of the cohort. Canada Post's definition of a rural address (a zero in the second position of the postal code) was used to characterize each patient's residence as rural or urban.

The RAMQ database was used to obtain data on each cardiac catheterization, percutaneous transluminal coronary angioplasty (PTCA), and coronary artery bypass graft surgery (CABG) performed during the follow-up period. Complete four-year survival data were obtained for 99.7 percent of the AMI cohort by merging data from both the Med-Echo and the RAMQ databases. The methods used to ascertain accurate survival data have been published elsewhere (19). All follow-up data spanned the years from January 1, 1988, to December 31, 1992.

This study received ethical approval from the McGill University Institutional Review Board.

## *Hospital Characteristics*

As a preliminary step in the creation of the instrumental variables, we classified each acute care hospital in Quebec in four ways: according to whether or not they had (1) availability of cardiac catheterization, (2) availability of PTCA, (3) availability of CABG, and (4) treated a high or low volume of first AMI patients during 1988. In 1988, there were 129 acute care hospitals admitting AMI patients in Quebec, and 13 (10 percent) offered cardiac catheterization. Of these 13 hospitals, 12 offered PTCA and 9 offered CABG. Thus, the hospital categories were not mutually exclusive.

To classify a hospital according to volume, we calculated the number of first AMI patients admitted in 1988 for each hospital. We classified any hospital treating a number of first AMI patients greater than or equal to the 75th percentile value for the distribution across all hospitals as a high-volume hospital.

The type of hospital of admission was classified based on the patient's initial hospitalization for AMI. Thus, if an AMI patient was admitted to a hospital without catheterization facilities and then later transferred to a hospital with catheterization facilities, the patient was considered admitted to a hospital without catheterization.

### *Instrumental Variables*

Similar to the approach used previously for the U.S. Medicare population (McClellan, McNeil, and Newhouse 1994), the four instrumental variables used in our study corresponded to the subjects' "differential distances" to the four classifications of hospitals. One instrumental variable corresponded to the subjects' differential distance to a catheterization hospital. We created this variable by calculating the difference between the distance from a subject's residence to the nearest catheterization hospital, and the distance from this subject's residence to the nearest acute care hospital of any type. The three other instrumental variables corresponded to the difference between the distance from a subject's residence to (1) the nearest CABG hospital, (2) the nearest PTCA hospital, and (3) the nearest high-volume hospital, and the subject's distance to the nearest acute care hospital of any type. The choice of these instrumental variables was based on two main assumptions: (1) that AMI patients who lived relatively closer to catheterization, PTCA, CABG, or high-volume hospitals were more likely to receive aggressive care, and (2) that differential distances to each hospital type were not associated with any characteristics such as health status, which could be associated with the receipt of aggressive care and mortality.

To construct the instrumental variables, we collected latitude and longitude data from Statistics Canada. We used spherical geographic coordinates derived from these data to construct straight-line distances from the center of each patient's residential postal code region to the center of the postal code regions for each acute care hospital in Quebec. Previous work suggests that these straight-line distances are highly correlated with travel time (Phibbs and Luft 1995).

*Analytic Approach*

To permit direct comparisons, the analytic approach was almost identical to that used for analyses applied to the U.S. Medicare population (McClellan, McNeil, and Newhouse 1994). The main independent variable used in this study was a binary variable corresponding to whether or not subjects received cardiac catheterization within 90 days after their admission for AMI. Receipt of this procedure was used to indicate the receipt of aggressive care. Our data show that most AMI patients in Quebec who receive catheterization will receive this procedure within 90 days (median time in 1988 = 34 days). In addition, only small numbers of patients will sustain a recurrent AMI within this time period (7 percent in 1988).

There were seven outcome variables used in this study: binary variables corresponding to mortality at 1 day, 7 days, 30 days, and 1, 2, 3 and 4 years following the date of admission for AMI.

As a first step in the analytic approach, we compared demographic characteristics, comorbid diseases, invasive procedures received, and mortality between subjects who received cardiac catheterization within 90 days and subjects who did not.

Second, we used a standard statistical method—analysis of variance (ANOVA)—to estimate the association between catheterization within 90 days, and mortality. For each mortality variable, we created a model that adjusted for age, sex, rural or urban residence, and comorbid diseases.

Third, we placed subjects into two groups based on their differential distance to each type of hospital—"high" and "low" differential distance. We then compared the demographic and clinical characteristics of each group, as well as the invasive procedures received and mortality, across each differential distance group.

Finally, we used two-stage least squares regression analysis to estimate the average marginal effects of the aggressive approach to post-AMI care on mortality. For these analyses, we created four new sets of instrumental variables. Each set of instrumental variables corresponded to groups of subjects based on their differential distance to one of the four hospital types. For example, we created eight binary variables to form eight approximately equal-sized groups of subjects based on their differential distances to catheterization hospitals. Each variable was coded as 1 if the subjects' differential distance to a catheterization hospital fell within a specified range (in miles [1 mile = 1.61 km] and rounded off: 0, 0.02–1.7, 1.7–2.8, 2.9–5.2, 5.4–18.7, 18.8–35.1, 35.3–67.4, 68.2–473.0), and 0 otherwise. We also created eight binary variables based on subjects' differential distances to CABG and PTCA hospitals. Because the differential distance groups for PTCA hospitals had ranges identical to those for catheterization hospitals (in miles and rounded off: 0, 0.02–1.7, 1.7–2.8, 2.9–5.2, 5.4–18.7, 18.8–35.1, 35.3–67.4, 68.2–473.0), we did not include the groups for PTCA hospitals in any subsequent analyses. We created three binary variables based on subjects' differential distance to a high-volume hospital (in miles and rounded off: 0, 0.05–5.5, 5.6–531.6).

Before running our two-stage least squares regression models, we examined $F$-statistics for the association between the instrumental variables and receipt of catheterization (first-stage regression equations). All $F$-statistics for patients of all ages were 13.6 or greater (range: 13.6–34.7). The models including receipt of catheterization within one day as an outcome measure, and the models examining only study subjects either $<65$ years old or $\geq 65$ years old, corresponded with lower $F$-statistics. However, all models corresponded with a $p$-value $<.05$, except for some of the models including receipt of catheterization within one day as an outcome measure (for study subjects $\geq 65$ years old). Mortality at one day after AMI was therefore not used as an outcome measure in the two-stage least squares regression analyses for subjects $\geq 65$ years old. These results provided evidence to support the hypothesis that differential distance to different types of hospitals is associated with aggressive care. The fact that the proportions of patients who received cardiac catheterization within 90 days decreased across greater differential distance groups provided additional evidence (data not shown).

The two-stage least squares regression models estimated the average effects of aggressive care on mortality for marginal subjects within the same age group, and with the same sex and comorbid diseases. We included different combinations of instrumental variables in the different regression models in order to account for differential access to aggressive care at catheterization, CABG, and high-volume hospitals both singularly and simultaneously. The main independent variables included in models estimating effects on mortality at 1 day, 7 days, and 30 days were receipt of catheterization within 1 day, 7 days, and 30 days, respectively. To evaluate the marginal effects of aspects of aggressive care other than invasive treatments, such as emergency response systems (McClellan, McNeil, and Newhouse 1994), some models also included rural residence or admission to a high-volume hospital as independent variables.

We completed each set of analyses for all study subjects, for subjects $<65$ years and $\geq 65$ years of age at the time of admission for AMI. We performed all analyses using *STATA* 4.0 (Stata Press, College Station, Texas).

# RESULTS

### Study Population

Our final study population consisted of 8,674 subjects (96.43 percent of the original AMI cohort). A total of 1,928 subjects (22 percent) received cardiac catheterization within 90 days after admission. A total of 51 percent of subjects were $\geq$65 years old at the time of admission. Fewer of these elderly subjects received cardiac catheterization within 90 days in comparison with subjects $<$65 years old (11 percent versus 34 percent).

There were marked differences in demographic characteristics, comorbid diseases, and characteristics of care received between subjects who received catheterization within 90 days and subjects who did not (Table 1). Subjects who received catheterization were younger on average, and smaller proportions were female and resided in rural areas. In addition, smaller proportions of subjects who received catheterization had comorbid diseases. Greater proportions of subjects who received catheterization were admitted to catheterization, PTCA, CABG, and high-volume hospitals, and greater proportions of these subjects received CAGB or PTCA within 90 days.

### Standard Outcome Measures and Evidence for Confounding Bias

There were large differences in mortality between subjects who received catheterization within 90 days and subjects who did not (Table 1). By four years following admission for AMI, only 14 percent of subjects who received catheterization within 90 days had died, while 41 percent of subjects who did not receive catheterization had died. After adjusting these differences for observable subject characteristics, the percentage-point differences in four-year mortality rates between the two groups was reduced from 28 percent to 13 percent (Table 2, in the online appendix, which is available at http://blackwellpublishing.com/products/journals/suppmat/HESR/HESR02099/HESR02099sm.htm). However, given the marked differences between the groups in terms of observable characteristics, it is likely that there were also many other differences between the groups in terms of characteristics that were not captured in the database, such as AMI severity or acute complications. It is therefore likely that these adjusted outcome measures overestimate the true effects of aggressive care. In addition, differences in mortality between the two groups were evident only one day after admission for AMI (adjusted difference of 4 percent; 95 percent CI: 3 percent to 5 percent), when catheterization was not likely to have already been received.

Table 1: Characteristics of Patients with a First Acute Myocardial Infarction in Quebec in 1988

| | *No Catheterization within 90 Days (n = 6,746)* | *Catheterization within 90 Days (n = 1,928)* | *Unadjusted Difference (95% CI)* |
|---|---|---|---|
| **Demographic characteristics** (%) | | | |
| Female | 36 | 23 | 13 (11,16) |
| Mean age in years (SD) | 66 (13) | 56 (11) | 10 (9,10) |
| Rural residence | 27 | 21 | 5 (3,7) |
| **Comorbid diseases** (%) | | | |
| Cancer | 1 | 0 | 1 (1,1) |
| Pulmonary disease, uncomplicated | 12 | 6 | 6 (5,8) |
| Dementia | 1 | 0 | 1 (1,1) |
| Diabetes | 18 | 13 | 5 (3,7) |
| Renal disease, uncomplicated | 4 | 2 | 2 (1,3) |
| Cerebrovascular disease | 6 | 2 | 4 (3,4) |
| **Care received** (%) | | | |
| Initial admit to catheterization hospital[1] | 19 | 39 | – 20 (– 22, – 18) |
| Initial admit to PTCA hospital[2] | 17 | 33 | – 16 (– 18, – 14) |
| Initial admit to CABG hospital[3] | 14 | 27 | – 13 (– 16, – 11) |
| Initial admit to high-volume[†] hospital[4] | 58 | 73 | – 15 (– 17, – 13) |
| Catheterization within 7 days | 0 | 32 | – 32 (– 34, – 30) |
| CABG within 90 days | 0 | 17 | – 17 (– 19, – 16) |
| PTCA within 90 days | 3 | 18 | – 16 (– 17, – 14) |
| **Cumulative mortality** (%) | | | |
| 1 day | 6 | 0 | 6 (5,6) |
| 7 days | 13 | 1 | 12 (11,13) |
| 30 days | 18 | 3 | 16 (14,17) |
| 1 year | 27 | 7 | 20 (19,22) |
| 2 years | 33 | 9 | 24 (22,25) |
| 3 years | 37 | 12 | 26 (24,28) |
| 4 years | 41 | 14 | 28 (26,29) |

CABG denotes coronary artery bypass graft, PTCA denotes percutaneous transluminal coronary angioplasty.

All acute care hospitals in Quebec were classified according to availability of catheterization[1], PTCA[2], and/or CABG[3], as well as number of patients admitted for a first acute myocardial infarction in 1988.[4] Hospital categories were not mutually exclusive.

[†]At least 133 admissions for first acute myocardial infarction in 1988.

### *Unadjusted Comparisons across Differential Distance Groups*

Two groups of subjects were formed based on the median differential distance to a catheterization hospital. Comparisons of demographic characteristics and comorbid diseases across these differential distance groups (Table 3) showed differences that were substantially less marked than those observed when comparing according to the receipt of catheterization. Only small differences were found despite the fact that a greater proportion of patients in the low-differential distance group received catheterization within 90 days (26 percent versus 19 percent). As would be expected, greater proportions of subjects in the low-differential distance group were admitted to catheterization, PTCA, CABG, and high-volume hospitals, and greater proportions of these subjects received PTCA and CABG. These results provide support for the assumption that a subject's differential distance to a catheterization hospital is associated with their receipt of catheterization, but is not associated with other characteristics that could influence selection for receipt of catheterization, such as age and comorbid diseases. Finally, unlike the large mortality differences observed in Table 2 (available on-line only), there were no differences in mortality observed across the differential distance groups at any time period.

*Instrumental Variable Estimation: Two-Stage Least Squares Regression Analysis*

The instrumental variable estimates of marginal effects of aggressive care suggest that, on the margin, there are no mortality benefits from receipt of aggressive care (Table 4). All confidence intervals included zero. For example, in the simplest model, which included only sets of instrumental variables corresponding to differential distance to catheterization hospitals, the average difference in mortality at three years was $-4$ percent (favoring receipt of catheterization; 95 percent CI: $-20$ percent to 13 percent). In the full model, which contained three sets of instrumental variables (differential distances to catheterization, CABG, and high-volume hospitals) and examined the effects of both admission to a high-volume hospital and catheterization simultaneously, the average difference in mortality at three years was also $-4$ percent (favoring receipt of catheterization and admission to a high-volume hospital; 95 percent CI: $-29$ percent to 22 percent). The results do not show any notable trends according to timing after AMI. Finally, admission to a high-volume hospital (Table 4) and rural residence (data not shown) was not associated with mortality.

*Marginal Effects of Aggressive Care in Canada versus the United States*

By examining data for subjects $\geq$65 years old at the time of their admission for AMI, we were able to directly compare the marginal effects of aggressive care on mortality in Quebec with estimates reported for the United States (McClellan, McNeil, and Newhouse 1994). Table 5 shows that the trends in the demographic, comorbid disease, treatment, and mortality differences

Table 3: Patient Characteristics by Differential Distance* to a Catheterization Hospital

| | *Differential Distance ≤5.2 Miles (n = 4,334)* | *Differential Distance > 5.2 Miles (n = 4,340)* | *Unadjusted Difference (95% CI)* |
|---|---|---|---|
| **Demographic characteristics** (%) | | | |
| Female | 36 | 31 | 5 (3,7) |
| Mean age in years (SD) | 65 (13) | 63 (13) | 1 (1,2) |
| Rural residence | 6 | 45 | − 39 ( − 41, − 37) |
| **Comorbid diseases** (%) | | | |
| Cancer | 1 | 1 | 0 (0,1) |
| Pulmonary disease, uncomplicated | 10 | 12 | −2 ( − 4, − 1) |
| Dementia | 1 | 0 | 0 (0,0) |
| Diabetes | 18 | 16 | 2 (0,3) |
| Renal disease, uncomplicated | 4 | 2 | 2 (1,2) |
| Cerebrovascular disease | 5 | 5 | 1 (0,2) |
| **Care received** (%) | | | |
| Initial admit to catheterization hospital[1] | 39 | 7 | 32 (30,33) |
| Initial admit to PTCA hospital[2] | 35 | 7 | 28 (26,30) |
| Initial admit to CABG hospital[3] | 28 | 6 | 22 (21,24) |
| Initial admit to high-volume[†] hospital[4] | 76 | 47 | 29 (27,31) |
| Catheterization within 7 days | 10 | 4 | 5 (4,6) |
| Catheterization within 90 days | 26 | 19 | 7 (5,9) |
| CABG within 90 days | 4 | 4 | 1 (0,2) |
| PTCA within 90 days | 7 | 5 | 2 (1,3) |
| **Cumulative mortality** (%) | | | |
| 1 day | 4 | 5 | 0 ( − 1,1) |
| 7 days | 10 | 10 | 1 ( − 1,2) |
| 30 days | 15 | 14 | 1 ( − 1,2) |
| 1 year | 23 | 22 | 1 (0,3) |
| 2 years | 28 | 27 | 1 ( − 1,3) |
| 3 years | 32 | 31 | 1 ( − 1,3) |
| 4 years | 36 | 35 | 1 ( − 1,3) |

CABG denotes coronary artery bypass graft, PTCA denotes percutaneous transluminal coronary angioplasty.

All acute care hospitals in Quebec were classified according to availability of catheterization[1], PTCA[2], and/or CABG[3], as well as number of patients admitted for a first acute myocardial infarction in 1988.[4] Hospital categories were not mutually exclusive.

[†]At least 133 admissions for first acute myocardial infarction in 1988.

*Median differential difference to a catheterization hospital.

across high- and low-differential groups were similar in Quebec and the United States. Data from both sources showed no large average differences in mortality across the high- and low-differential distance groups. Instrumental variable estimation showed no marginal benefits from receipt of catheterization in Quebec patients $\geq$65 years old, while small marginal benefits were shown for the U.S. Medicare population (Table 6).

*Marginal Effects of Aggressive Care in Younger versus Older AMI Patients*

The trends in the differences in demographic characteristics, comorbid diseases, and care received between high- and low-differential distance groups were similar for both subjects $\geq$65 years old (Table 5) and subjects $<$65 years old (data not shown). Both the two-group comparisons across high- and low-differential distance groups and the two-stage least squares regression analyses (Table 6, available on-line only) showed no effects of receipt of catheterization on mortality in either younger or older subjects.

## DISCUSSION

In this study, we applied instrumental variable methodology to evaluate the effectiveness of an aggressive approach to AMI care in a Canadian patient population. We found that an aggressive approach was not associated with marginal mortality benefits up to four years after the AMI in both elderly and younger patients. The trends observed in differences across the comparison groups in subject characteristics and care received were consistent with those obtained by applying the same methodology to a population of elderly U.S. Medicare beneficiaries (McClellan, McNeil, and Newhouse 1994), giving face validity to the methodology. However, our mortality results are inconsistent with the United States study, which found small marginal mortality benefits resulting from more aggressive care. These results are also contrary to our hypothesis that the marginal benefits of aggressive care should be greater in the Canadian patient population, where the approach to care is more conservative overall.

The results of this study are consistent with those from previous randomized controlled trials (Barbash et al. 1990; Rogers et al. 1990; Simoons et al. 1988; TIMI Study Group 1989) and observational studies (Pilote, Racine, Hlatky 1994; Mark et al. 1994). This study therefore provides evidence that aggressive care after AMI may not be beneficial except for patients with specific indications for invasive cardiac procedures ("ACC/AHA Guidelines" 1996; Ryan et al. 1999). The fact that our results are generalizable across AMI patient populations of all ages provides support for this conclusion.

Studies have shown that rates of use of invasive procedures are increasing overall both in the United States (Pilote et al. 1998) and in Canada

Table 4: Adjusted Estimates of Marginal Effects of an Aggressive Approach to Care after Acute Myocardial Infarction on Mortality: Two-Stage Least Square Regression Analyses Including Instrumental Variables

| | | | *Marginal Differences (%) in Mortality (95% Confidence Interval)* | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| *Model** | *Instrumental Variables*** | *Independent Variable(s)* | *1-Day* | *7-Day* | *30-Day* | *1-Year* | *2-Year* | *3-Year* | *4-Year* |
| 1 | CATH | Catheterization received | – 14 (– 82,54) | 1 (– 14,16) | 0 (– 12,13) | 4 (– 11,20) | 2 (– 15,18) | – 4 (– 20,13) | – 9 (– 26,8) |
| 2 | CATH<br>CABG | Catheterization received | – 9 (– 74,56) | 3 (– 12,17) | 0 (– 12,12) | 4 (– 11,20) | 1 (– 15,18) | – 4 (– 21,13) | – 10 (– 27,7) |
| 3 | CATH | Admit to high-volume hospital | 0 (– 2,1) | 0 (– 3,2) | – 1 (– 5,2) | – 2 (– 6,3) | 0 (– 4,4) | 0 (– 4,4) | 1 (– 4,5) |
| | CABG<br>High-volume | Catheterization received | – 9 (– 64,46) | 5 (– 13,22) | 4 (– 14,22) | 11 (– 13,35) | 3 (– 22,28) | – 4 (– 29,22) | – 12 (– 38,13) |

CATH denotes cardiac catheterization, CABG denotes coronary artery bypass graft surgery.

*Results from some models not shown.

**Instrumental variables used in analyses were differential distances to the nearest catheterization hospital (CATH), CABG hospital (CABG), or high-volume hospital. Other variables included in each model were age group, sex, and comorbid diseases.

Table 5: Patient Characteristics According to Differential Distance* to a Catheterization Hospital for Patients ≥65 Years Old in Quebec and the United States

| | *Quebec* | | *United States*** | |
|---|---|---|---|---|
| | *Differential Distance ≤4.7 miles n = 2,212* | *Differential Distance > 4.7 miles n = 2,210* | *Differential Distance ≤2.5 miles n = 102,516* | *Differential Distance > 2.5 miles n = 102,505* |
| **Demographic characteristics** (%) | | | | |
| Female | NA | NA | 51 | 50 |
| Mean age in years (SD) | 75 (7) | 74 (6) | 76 (7) | 76 (7) |
| Rural residence | NA | NA | 7 | 52 |
| **Co-morbid diseases** (%) | | | | |
| Cancer | 2 | 2 | 2 | 2 |
| Pulmonary disease, uncomplicated | 12 | 15 | 10 | 11 |
| Dementia | 1 | 1 | 1 | 1 |
| Diabetes | 21 | 20 | 18 | 18 |
| Renal disease, uncomplicated | 6 | 4 | 2 | 2 |
| Cerebrovascular disease | 7 | 8 | 5 | 5 |
| **Care received** (%) | | | | |
| Initial admit to catheterization hospital[1] | NA | NA | 34 | 5 |
| Initial admit to PTCA*** hospital[2] | NA | NA | 42 | 11 |
| Initial admit to CABG*** hospital[3] | NA | NA | | |
| Initial admit to high-volume† hospital[4] | NA | NA | 67 | 37 |
| Catheterization within 7 days | NA | NA | 21 | 11 |
| Catheterization within 90 days | NA | NA | 26 | 20 |
| CABG within 90 days | NA | NA | 9 | 7 |
| PTCA within 90 days | NA | NA | 6 | 4 |
| **Cumulative mortality** (%) | | | | |
| 1 day | NA | NA | 8 | 9 |
| 7 days | NA | NA | 17 | 19 |
| 1 year | NA | NA | 40 | 41 |
| 2 years | NA | NA | 47 | 48 |
| 3 years | NA | NA | 53 | 54 |
| 4 years | NA | NA | 58 | 59 |

CABG denotes coronary artery bypass graft, PTCA denotes percutaneous transluminal coronary angioplasty.

All acute care hospitals in Quebec were classified according to availability of catheterization[1], PTCA[2], and/or CABG[3], as well as number of patients admitted for a first acute myocardial infarction in 1988[4]. Hospital categories were not mutually exclusive.

*Median differential difference to a catheterization hospital in Quebec was 4.7 miles. Median differential distance to a catheterization hospital in the United States was 2.5 miles.

***All hospitals in the United States with availability of either CABG or PTCA were classified as "revascularization hospitals."

†At least 133 admission for first acute myocardial infarction in 1988 for Quebec hospitals. At least 75 admissions for first acute myocardial infarction in 1987 for United States hospitals.

(Pilote et al. 2000). In fact, a recent study suggests rates of use of invasive procedures in some regions of Quebec are approaching those in the United States (Pilote et al. 2002). Thus, the present study should be of interest to clinicians and policymakers who question whether invasive cardiac procedures are under- or overutilized in certain regions.

More generally, the results of this study should be of interest to investigators interested in evaluating the effectiveness of health interventions using administrative data. As in the study by McClellan, McNeil, and Newhouse (1994), we found evidence to suggest that outcome measures obtained using standard statistical measures were subject to confounding bias and that outcome measures obtained using the instrumental variable methodology were likely to be less biased. This evidence highlights the potential usefulness of instrumental variables as a methodologic tool.

There are several limitations to the instrumental variable approach that must be considered. One limitation is that instrumental variable estimates are less precise than estimates obtained from other methods (Zohoori and Savitz 1997; Gowrisankaran and Town 1999; "Econometric Issues for Survey Data" 1997). For instance, the confidence intervals around our adjusted outcome measures were wide. This lack of precision was probably due to the relatively small numbers of patients receiving invasive procedures in Quebec. However, even analyses applying this methodology to a greater number of AMI patients admitted in Quebec (over the years from 1988 to 1995) did not provide estimates with substantially more precision (data not shown). Since Quebec represents roughly one-fourth of the Canadian population, even an expansion of this study across Canada is unlikely to sufficiently improve the efficiency of the outcome measures. An international study that accounts for variations across regions in approaches to post-AMI care may provide more efficient estimates. In the case of our study, instrumental variables estimates were a good alternative to standard outcome measures that were likely strongly biased.

The instrumental variables approach is also limited in that although the validity of the assumptions made in choosing the instrumental variables used in a study is crucial (Harris and Remler 1998; "Econometric Issues for Survey Data" 1997), this validity cannot be proven. For instance, our comparisons of demographic characteristics and comorbid diseases across low- and high-differential distance groups provided evidence that subjects did not differ substantially in terms of these observed characteristics. However, we cannot rule out the possibility that the subjects differed in terms of other unobserved characteristics.

In summary, we observed that there was no association between a more aggressive approach to post-AMI care and short- or long-term mortality in marginal patients admitted for AMI in Quebec. Thus, this study cannot lend support to the conclusion that expanding the aggressive approach to post-AMI care beyond current levels would provide benefits. However, because the small potential benefits suggested by our point estimates may prove to be clinically, if not statistically, significant, a larger international study is warranted to improve the statistical efficiency of outcome measures obtained using instrumental variable methodology.

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Table 2: Cumulative Effects of Catheterization within 90 Days after Acute Myocardial Infarction* on Mortality, Not Accounting for Bias Due to Unobserved Differences between Patients Receiving and Not Receiving Catheterization

| | *Percentage-Point Changes in Mortality Rates (95% CI)* | | | | | | |
|---|---|---|---|---|---|---|---|
| | *1-Day* | *7-Day* | *30-Day* | *1-Year* | *2-Year* | *3-Year* | *4-Year* |
| None (unadjusted differences) | – 6 (– 7, – 5) | – 12 (– 14, – 11) | – 16 (– 17, – 14) | – 20 (– 22, – 18) | – 24 (– 26, – 21) | – 26 (– 28, – 24) | – 28 (– 30, – 25) |
| After adjustment for age, sex and rural or urban residence | – 4 (– 5, – 3) | – 8 (– 10, – 6) | – 10 (– 11, – 8) | – 11 (– 13, – 9) | – 13 (– 15, – 11) | – 14 (– 16, – 11) | – 14 (– 16, – 12) |
| After adjustment for age, sex, rural or urban residence and comorbid diseases | – 4 (– 5, – 3) | – 8 (– 10, – 6) | – 9 (– 11, – 8) | – 10 (– 12, – 8) | – 12 (– 14, – 10) | – 13 (– 15, – 10) | – 13 (– 15, – 11) |

*Analyses were performed using *ANOVA*.

Table 6: Adjusted Estimates of Marginal Effects of an Aggressive Approach to Care after Acute Myocardial Infarction on Mortality in Elderly (≥65 Years) and Younger (<65 Years) Patients: Two-Stage Least Squares Regression Analyses Including Instrumental Variables

| | | | *Marginal Differences (%) in Mortality (95% Confidence Interval)* | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| *Model** | *Instrumental Variables*** | *Independent Variable(s)* | *1-Day* | *7-Day* | *30-Day* | *1-Year* | *2-Year* | *3-Year* | *4-Year* |
| | *Elderly Patients* | | | | | | | | |
| 1 | CATH | Catheterization received | NA | – 2 ( – 41,37) | – 7 ( – 44,29) | 3 ( – 38,45) | 5 ( – 37,48) | – 4 ( – 47,39) | – 20 ( – 63,23) |
| 2 | CATH | Catheterization received | NA | – 4 ( – 42,34) | – 20 ( – 54,13) | – 2 ( – 40,36) | – 1 ( – 40,37) | – 10 ( – 48,29) | – 27 ( – 66,12) |
| | CABG | | | | | | | | |
| 3 | CATH | Admit to high-volume hospital | NA | 0 ( – 3,4) | 0 ( – 4,5) | 0 ( – 5,5) | 2 ( – 3,8) | 2 ( – 3,7) | 1 ( – 4,7) |
| | CABG | | | | | | | | |
| | High-volume | Catheterization received | NA | – 6 ( – 47,35) | – 22 ( – 62,18) | – 2 ( – 46,41) | – 11 ( – 56,34) | – 17 ( – 62,28) | – 34 ( – 79,12) |
| | *Younger Patients* | | | | | | | | |
| 1 | CATH | Catheterization received | – 9 ( – 55,37) | 0 ( – 11,11) | – 1 ( – 9,8) | – 3 ( – 15,8) | – 8 ( – 21,5) | – 11 ( – 25,3) | – 13 ( – 28,1) |
| 2 | CATH | Catheterization received | – 15 ( – 57,26) | 0 ( – 10,11) | 0 ( – 8,9) | – 3 ( – 15,9) | – 8 ( – 21,5) | – 11 ( – 25,3) | – 13 ( – 27,1) |
| | CABG | | | | | | | | |
| 3 | CATH | Admit to high-volume hospital | 0 ( – 2,1) | – 1 ( – 4,1) | – 2 ( – 6,2) | – 1 ( – 6,4) | 0 ( – 5,5) | 0 ( – 5,6) | 2 ( – 4,8) |
| | CABG | | | | | | | | |
| | High-volume | Catheterization received | – 13 ( – 55,30) | 3 ( – 9,16) | 5 ( – 8,18) | 1 ( – 19,21) | – 7 ( – 28,15) | – 11 ( – 34,12) | – 18 ( – 43,6) |

CATH denotes cardiac catheterization, CABG denotes coronary artery bypass graft surgery.

"NA" denotes not applicable because F-tests for first-stage regressions were not significant; *Results from some models not shown.

**Instrumental variables used in analyses were differential distances to the nearest catheterization hospital (CATH), CABG hospital (CABG), or high-volume hospital. Other variables included in each model were age group, sex, and comorbid diseases.