Reviewer's report

Title: Impact of on-site cardiac catheterization on resource utilization and fatal and non-fatal outcomes after acute myocardial infarction

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Reviewer: William B Hillegass

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General

MS: Impact of On-site Cardiac Catheterization on Resource Utilization and Fatal and Non-fatal Outcomes after Acute Myocardial Infarction.

Halabi et al.

The authors report a large database analysis from the Quebec healthcare system that compares acute MI patients initially treated at hospitals with and without on-site cardiac catheterization laboratories from 1996 to 3/1999. They compare subsequent outcomes including death, readmission for MI/unstable angina/CHF and use of noninvasive tests, prescription medications, and invasive procedures/revascularization procedures. They conclude that acute MI patients initially admitted at hospitals without onsite catheterization facilities do as well as those initially treated at hospitals with onsite catheterization facilities in terms of mortality and readmissions for subsequent cardiac events. There is a higher rate of invasive procedures in the patients initially admitted to the invasive-capable facilities although interestingly CABG is done more frequently by one year in the patients initially admitted with AMI to the noninvasive facilities. Although counter to the authorsâ€™ initial hypothesis, the invasive facilities (with more cardiologists) also used more noninvasive studies such as echocardiography and nuclear tests.

The strengths of this analysis are that it is a population study with large numbers, the sophisticated approaches used to try to correct for the inherent biases and data limitations of administrative databases that lack pertinent clinical details, and the known expertise of the authors.

While the analysis is almost certainly internally correct, some of the initial hypotheses and conclusions need to be viewed with considerable caution due to the many limitations of the data and significant potential biases. The authorsâ€™ final conclusion is that these results suggest that a less invasive strategy following AMI appears to provide similar outcomes at a considerably lower use of resources. I think this conclusion is overreaching given the limitations of their data. I specifically object to the notion that this analysis should be construed as a comparison of an invasive approach versus more conservative approach in the care of acute myocardial infarction patients. I would recommend that the analysis not be published in its present form unless this implication is significantly modified because it is a potentially misleading and harmful contribution to the medical literature if published as is. There are several concerns and questions about the data that the authors should further address.

â€¢ The result does not square with the weight of the evidence from recent prospective randomized trials and meta-analyses/meta-regressions of these randomized trials. This body of evidence would STRONGLY suggest (actually have proven) the mortality benefit and reduction in major adverse cardiac and cerebrovascular events (e.g., stroke, reinfarction) in patients receiving an early invasive approach for acute ST-elevation MI. Similarly, the bulk of the evidence from modern RCTs would suggest a reduction in nonfatal cardiovascular events in NSTEMI acute coronary syndrome patients receiving an early invasive approach: FRISCII, VINO, TACTICS-TIMI 18, RITA with the only opposing trial being VANQWISH (dated and flawed). More recently the ICTUS trial in the Netherlands showed fewer readmissions for the routine early invasive strategy albeit a very high proportion of the early conservative group with mandated noninvasive risk-stratification crossed-over and received invasive evaluation and revascularization during the index hospitalization. So how do we explain this discrepancy in the findings? Perhaps it is simply the difference between efficacy in large but more select populations in RCTs versus effectiveness in the real world as the authors imply. I think more likely, however, the difference arises from the inability to control for all the biases without more detailed clinical data about the patients and the very low rate of application of an invasive strategy even in those patients presenting initially to the hospitals with on-site catheterization facilities.
The authors should provide more information on the type and severity of AMIs. Data on the treatment and time of treatments from initial presentation by type of MI as a function of hospital type at presentation would help us understand the data. The data as presented does not give even the close reader a sense of the management strategies employed as a function of whether the patient has a STEMI or NSTEMI/ACS. Is the population in this analysis all STEMI? If so, it seems like the rates of application of thrombolytics, salvage PCI, transfer, and primary PCI by hospital type at initial presentation should be specified to allow the reader to understand the management strategies used in Quebec during this time period. If the cohort includes NSTEMI/ACS patients, this should be specified and the management of these patients should also be specified (including transfer rates) as a function of hospital type at presentation. Since the diagnosis of acute MI as opposed to ruled out unstable angina or nonischemic chest discomfort syndrome is primarily a retrospective diagnosis based on biomarkers, how was this handled in selecting the patient population for the study cohort? Also it has been demonstrated that the rate of progressing to infarction in patients presenting with NSTEMI is reduced with an early invasive strategy. If a patient presented with unstable angina and an invasive strategy yielded resolution of the acute coronary syndrome with negative biomarkers, would this patient be excluded from the cohort because they did not have an MI? If they are excluded, this significantly biases the result against an invasive strategy since the most successfully treated cases would be excluded.

For the STEMI patients, it has been incontrovertibly proven that primary PCI saves lives plus reduces future events compared to both thrombolysis and non-lytic therapy. It has also been proven in the stent era that salvage PCI reduces mortality and subsequent events in the patients who fail lytics. How many of the patients had STEMI and received lytics at noninvasive facilities? Clearly very few patients were transferred for primary PCI or rescue PCI from the noninvasive hospitals. Furthermore, unless this cohort includes predominantly NSTEMI patients or lytics were widely used, very few patients at the facilities with onsite catheterization laboratories went for primary PCI.

Again, we are not provided with information on the rate of transfer of patients from the noninvasive to invasive facilities. (In the analysis, transfers are handled by assigning the patients and their outcomes to the hospital where they initially presented. While I agree this is the reasonable way to do the analysis, it would be very informative to break-out the results for the AMI patients presenting to hospitals without cath labs who are and are not transferred.) In addition, the cardiogenic shock sub-group should have this information displayed.

The care patterns at the hospitals with catheterization facilities are not specified. It is not specified whether the facilities with catheterization laboratories all perform PCI and CABG. This needs to be clarified. For the purposes of my review, I am making the assumption that the hospitals with cath labs also have PCI and cardiac surgery. Furthermore, it is not stated whether the hospitals with catheterization labs routinely performed primary PCI for STEMI. It is not at all clear that the hospitals with catheterization facilities followed an invasive strategy in the STEMI or NSTEMI patients, which is the treatment strategy demonstrated to have benefit in RCTs for both groups. Even if an invasive strategy was pursued, whether it was an early invasive strategy, i.e., time to treatment from presentation, is not specified. This is important because the benefit of an invasive strategy is greatest when it is a truly early invasive strategy in both STEMI and NSTEMI ACS. The existence of a catheterization laboratory at a hospital should not be assumed to indicate that the care pattern is an optimal utilization of an early invasive strategy.

During the time period of the study an early invasive strategy was not performed at most PCI-capable hospitals for NSTEMI patients since the convincing RCT data supporting this approach was not available at the time. In fact, it is clear from the data presented that even an invasive approach (let alone an early invasive approach) was not pursued in the hospitals with catheterization labs since only 35.1% of the patients presenting to these facilities underwent a catheterization during the index hospitalization. The catheterization rates in the conservative strategy arms of some of the RCTs is higher than the observed rate for patients presenting to an invasive capable facility in Quebec Province in the time period of this study. Although not an expert on the Canadian healthcare system, it is my understanding from discussions with several prominent Canadian interventionalists that they are very resource constrained to pursue a routine invasive approach with limited budgets that reduce use of stents and IIb/IIIa receptor antagonists. Given the very low utilization rate of catheterization and revascularization at the hospitals with catheterization laboratories in this study, it is not valid for the authors to draw any conclusions about the utility of an invasive approach. Furthermore, we need to know more about the time to treatment even in the minority of patients that received an invasive study who initially presented to a hospital with a cath lab to understand the outcomes.

The main nonfatal outcome affected by PCI is angina. Angina status post-MI is unknown in this
database. The authors show that the subsequent number of classes of anti-anginal medication used is no different between the patients initially presenting to hospitals with and without catheterization laboratories. It is not likely that this is a very valid surrogate measure for angina status for several reasons. First, all of these patients would be expected to be prescribed a beta-blocker for secondary prevention since they have had an MI regardless of angina status. CCBs are used more for hypertension than angina. But the major problem here is the bias that the patients sent to the invasive centers were significantly more likely to be evaluated by a cardiologist and have both invasive and noninvasive cardiac assessments leading to both mechanical and pharmacological treatments. We really have no measure as to whether the group managed with less noninvasive and invasive studies is being under treated and just living with more angina and silent ischemia than the group receiving more aggressive evaluation and, likely therefore, more aggressive treatment as well. Given the absence of adequate detailed measures of angina class, heart failure class, and/or functional status/quality of life measures, I believe the authors should be considerably more circumspect about the statement that the outcomes are similar. The measured outcomes may be similar but these are a rather limited picture of actual patient outcome.

The authors’ hypothesis that more invasive evaluation would lead to less noninvasive resource use in those patients has the flawed assumption that these tests are largely substitutes for each other. The example they provide is left ventriculography obviating the need for other noninvasive LV assessments. There are multiple reasons that both tests would be performed in a patient receiving appropriate care. For example, the left ventriculogram is often not performed in the setting of acute MI to limit contrast load in the face of renal insufficiency or unknown renal function, because of elevated LVEDP, because it may be the worst point in time to assess wall motion, etc. Often ECHO is needed for valvular function, to rule out LV thrombus, evaluate diastolic dysfunction, etc. Functional tests are also frequently needed to evaluate the functional significance of angiographic disease and myocardial viability to determine if revascularization is indicated. These tests are used more as complements in clinical practice than substitutes. It is not surprising that the patients evaluated at the more comprehensive cardiac facilities by cardiologists would have multiple tests performed to allow more complete evaluation of the patient. The impact of this on patient outcome is likely too subtle to be detected simply by readmissions for MI, UNSA, and CHF since stable angina and lesser degrees of CHF not requiring hospitalizations would be the main nonfatal outcomes influenced by the more aggressive mechanical and pharmacologic therapies. We get some hint of this with the lower readmission rate for unstable angina and mortality in the patients seen by a cardiologist as well as perhaps the lower CABG rate. AMI patients treated initially with a noninvasive approach who later have a catheterization because of angina have a higher rate of chronic infarct vessel occlusion that more frequently are addressed surgically instead of with PCI. What we usually observe with an early invasive approach is that acute total occlusions can be relatively easily opened with PCI at their initial presentation but become less suitable if the vessel remains occluded for more than two or three months after the infarct. This is likely the underlying phenomenon accounting for the authors’ observation.

Finally, as the authors point out, they have great difficulty dissecting the co-linearity of evaluation by a cardiologist and the presence of a catheterization laboratory. It is very striking in Table 1 that only 28.9% of the patients presenting to hospitals without catheterization facilities had their MI treated by a cardiologist. I suspect many of these were also the patients who were transferred. We do not know how many patients not transferred from without cath lab hospitals saw a cardiologist. I suspect from the data presented the answer is very few. This represents an enormous bias in treatment that does not seem separable from the cath lab present or absent characteristic of the hospital. This bias likely explains the resource utilization results. It has been demonstrated in other studies that patients with MI, CAD, or CHF are more likely to be treated to guidelines if a cardiologist is involved in their care with better clinical outcomes. The authors also note that care by a cardiologist results in better clinical outcomes. I am not certain that this bias can be corrected for because of the strong co-linearity between cardiologist care and onsite catheterization laboratory.

Overall, the analysis from this large dataset is almost certainly internally correct that utilization of both invasive and noninvasive resources in the care of AMI patients is greater at hospitals with on site catheterization laboratories and cardiologists. It appears, however, that during the timeframe of the cohort studied (1996-1999), that an invasive approach was applied in only a minority of the patients presenting to the hospitals with catheterization facilities. Subsequent RCTs have demonstrated a benefit of an early invasive approach in both STEMI and NSTEMI patients. Angina, heart failure, and functional status are not directly measured as perhaps the most important nonfatal outcomes likely to be affected by a more aggressive pharmacological and mechanical treatment strategy. There is suggestion of better outcome with treatment by a cardiologist with this factor having extensive co-linearity with the presence of an onsite catheterization laboratory. While an interesting dataset and analysis, robust and valid claims as to the lack of cost-effectiveness or impact on clinical outcomes of an invasive versus conservative approach to the care
of the acute MI patient should not be drawn from this data. I would not favor publication of this manuscript in its present form since the conclusions are quite suspect based on the limitations I have outlined. Given these limitations, I do not think this data is strong enough evidence to accept it as a legitimate and valid challenge to the opposite conclusions reached in contemporary RCTs and meta-analyses.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Please see all of above under general comments.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of limited interest

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Declaration of competing interests:

I declare that I have no competing interests.