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MANAGEMENT OF ACUTE CORONARY SYNDROMES (H JNEID, SECTION EDITOR)

Revascularization Strategies for Non-ST-Elevation Myocardial Infarction

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Abstract

Purpose of Review Non-ST-elevation myocardial infarction (NSTEMI) is an urgent medical condition that requires prompt application of simultaneous pharmacologic and non-pharmacologic therapies. The variation in patient clinical characteristics coupled with the multitude of treatment modalities makes optimal and timely management challenging. This review summarizes risk stratification of patients, the role and timing of revascularization, and highlights important considerations in the revascularization approach with attention to individual patient characteristics.

Recent Findings The early invasive management of NSTEMI has fostered a reduction in future ischemic events. Risk calculators are helpful in determining which patients should receive early invasive management. As many patients have multivessel disease, identifying the true culprit lesion can be challenging. Special attention should be given to those at the highest risk, such as diabetics, patients with renal failure, and those with left main disease.

Summary In patients with acute coronary syndrome, the decision and mode of revascularization should carefully integrate the patient's clinical characteristics as well as the complexity of the coronary anatomy.

Keywords Non-ST-elevation myocardial infarction · Revascularization · Review

Introduction

Non-ST-elevation myocardial infarctions (NSTEMI) represent a major subset of acute coronary syndromes and are a significant cause of morbidity and mortality for hundreds of thousands of US patients annually [1]. Data to support early invasive management have been adopted for over a decade, with evidence pointing to a reduction in subsequent ischemic events [2, 3]. Whether patients are treated with an early or ischemic-guided approach, coronary revascularization commonly ensues. Determining the mode of revascularization, be it percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) depends on patient-specific as well as anatomic considerations. Patient-specific factors include presence of diabetes, renal insufficiency, cerebrovascular disease, and other comorbidities that influence operative risk. Anatomical considerations primarily address feasibility of PCI, success rates, and risk of subsequent target vessel failure. Presence of left ventricular dysfunction and/or valvular abnormalities are other variables that play a significant role in decision-making.

Once all variables have been analyzed, a discussion with the patient regarding the benefit of revascularization and the risk of complications should follow. A shared decision-making process ensues. Depending on the anatomical details and application of the contemporary evidence, surgical revascularization may be a reasonable option, so the decision-making process should then incorporate a surgical opinion, what has typically been labeled the heart team approach. The ultimate goal is to provide a safe intervention (in this case a revascularization modality) that not only alleviates symptoms, but also decreases future morbidity and mortality. Traditionally, CABG has been the preferred method of

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revascularization for patients with extensive disease and specific comorbidities while percutaneous coronary intervention (PCI) has been preferred for patients with discrete coronary lesions. With advances in PCI equipment and techniques, these traditional and binary guidelines have been challenged. Drug-eluting stents (DES), particularly the second and third-generation devices have significantly reduced the risk of complications and target vessel failure [4, 5]. Potent antiplatelet therapies and high-potency statins not only contribute to early success but provide significant reduction in subsequent risk of ischemic events [6, 7]. Table 1 not only demonstrates the shifting clinical practice with higher percentages of patients referred to revascularization but also the steady increase in proportion of patients revascularized by PCI.

It is important to recognize that most randomized-controlled trials comparing the two modalities have a patient population who are eligible for both modes of revascularization, and thus often only address a subset of "real-world" patients. This paper will attempt to contemporize practical revascularization strategies and principles important to the management of NSTEMI.

Optimal Timing of Revascularization

The 2014 American College of Cardiology (ACC)/American Heart Association (AHA) Guidelines for the Management of Patients with NSTEMI recommend combining clinical history, physical examination, electrocardiogram (ECG), and cardiac biomarkers to make a rapid determination of the likelihood of obstructive coronary artery disease [8••]. Risk stratification after a diagnosis of NSTEMI is made a crucial first step in the management of such patients as risk stratification not only guides the heart team's decision on timing of revascularization but also provides patients with information regarding their prognosis. Patients with NSTEMI are at a widely varying risk of morbidity and mortality. The Thrombolysis in Myocardial Infarction (TIMI) and Global Registry of Acute Coronary Events (GRACE) scoring systems are two traditional models which have been used to facilitate triage and decision-making in NSTEMI patients [9, 10]. The more contemporary HEART score, which is predictive of the 6-week risk of major adverse cardiac events, may provide better prediction of events compared with TIMI and GRACE models [11, 12]. Furthermore, high-sensitivity troponin assays may help accelerate the management of patients as dynamic changes in troponin levels during serial sampling can help distinguish ischemic from non-ischemic causes of chest pain and mild cardiac enzyme leak. Incorporation of a high-sensitivity troponin should be embedded into the chest pain algorithm from the time the patient is seen in the emergency department. The rule-out safety and rule-in performance of a 0 and 1-h high-sensitivity troponin assessment demonstrated a sensitivity of 99.4% with a negative predictive value of 99.8% [13].

After initial risk assessment has been performed, the clinician's next step is to triage patients towards one of two broad pathways: an early-invasive or ischemia-driven pathway. While the aforementioned risk stratification tools can provide some level of decision-making support, individualization of management based on an overall clinical picture is paramount. It is important to identify unstable patients early and proceed with angiography on a more urgent/emergent (within 2 h) basis. These include those with persistent angina despite intensive attempts at medical therapy, dynamic ECG changes, hemodynamic instability, electrical instability, or those with severe left ventricular dysfunction or overt heart failure. Most stable NSTEMI patients will undergo a routine early invasive approach utilizing coronary angiography within 24–48 h of hospitalization. The ischemia-guided approach is practical for patients at low risk for in-hospital mortality and typically have no concerning ECG findings or only minimally detectable elevation in cardiac biomarkers.

Several studies have demonstrated that early angiography and revascularization are known to reduce the risk of

Table 1 Trends of revascularization in selected landmark acute coronary syndrome studies

Study	Year	Enrolled patients	% of cohort revascularized	PCI	CABG
TIMI IIIB	1995	1473	4.1%	59.0%	49.2%
VANQWISH	1998	920	36.4%	45.7%	54.3%
FRISC II	1999	2457	57.2%	52.8%	47.2%
TACTICS-TIMI 18	2001	2220	54.8%	65.4%	34.6%
CURE	2001	12,564	37.6%	56.2%	43.8%
RITA-3	2002	1810	43.0%	60.8%	39.2%
SYNERGY	2004	9978	65.7%	71.5%	28.5%
ACUITY	2006	13,819	67.5%	83.5%	16.5%
EARLY-ACS	2009	9406	72.1%	81.9%	18.1%
TIMACS	2009	3031	71.7%	80.1%	19.9%
PLATO	2009	18,624	74.5%	86.3%	13.7%

refractory ischemia, recurrent myocardial infarction, repeat hospitalization, and death [2, 14, 15] (Fig. 1).

According to the CathPCI Registry, more than 70% of all PCI procedures performed in 2017 were in patients with unstable angina (UA) or NSTEMI [16]. While coronary angiography in the setting of NSTEMI has increased, as per Medicare Provider Analysis and Review, there has been only a modest increase in the percent of NSTEMI patients receiving PCI during initial hospitalization (from 21.3% in 2002 to 33% in 2014). Roughly 8–10% of patients will undergo CABG, while the remainder receive conservative best-practice medical therapy [17]. Additionally, 32–40% of patients with a NSTEMI will undergo PCI [16]. The exact timing of PCI in hemodynamically stable NSTEMI patients remains a subject for debate. Earlier randomized trials demonstrated no difference in extent of myonecrosis or major adverse events between those treated within the first 2 h vs 24–48 h [18]. Another prospective randomized trial compared immediate (< 2 h), early (10–48 h), and selective angiography, again demonstrating no difference in major ischemic events at 6 months [19]. However, more recent data point to a reduction in major ischemic events, mostly new myocardial infarctions, in those subjected to angiography and revascularization within the first 2 h. In the RIDDLE-NSTEMI trial, 323 NSTEMI patients were randomized 1:1 to an immediate-intervention group (< 2 h after randomization) and a delayed-intervention group (2 to 72 h). The primary endpoint was the occurrence of death or new myocardial infarction (MI) at 30-day follow-up. That was achieved less frequently in patients undergoing immediate compared to delayed intervention (4.3% vs. 13%, $p = 0.008$), the difference primarily driven by excess new infarctions in the delayed intervention group [20]. A meta-analysis of eight randomized clinical trials addressing early versus delayed angiography and including more than 5000 patients followed for a median of 180 days does not show improved survival in all comers. It does however suggest that early angiography contributes to improved survival in certain subsets of high-risk patients such as those with positive biomarkers, higher GRACE scores, diabetes, or age of 75 years or older [21] (Fig. 2).

Current guidelines do not offer recommendations regarding the optimal timing of CABG in patients with NSTEMI. Early retrospective studies found that when CABG was performed earlier in patients with NSTEMI, there was a trend towards more significant in-hospital mortality, heart failure, MI, and cardiogenic shock [22–25]. However, in the largest cohort of patients who underwent CABG for NSTEMI, immediate CABG (performed within 24-h of diagnosis of NSTEMI) had similar long-term outcomes compared to delayed CABG (72 h after presentation) despite patients having higher risk profiles [26]. As NSTEMI is characterized by non-transmural necrosis, early revascularization may limit infarct expansion and possible progression to transmurality. However, randomized trial evidence for such findings after CABG for NSTEMI patients is not currently available.

Considerations for Revascularization

In single and most two-vessel disease patients, it is typically easier to decide in favor of a PCI approach to revascularization. However, when multivessel revascularization is necessary, strong consideration should be given to a surgical approach. As discussed, clinical and anatomic variables in addition to patient preferences all play a role in the shared decision-making process. Diabetes, for example, is an important clinical variable that should guide management and is

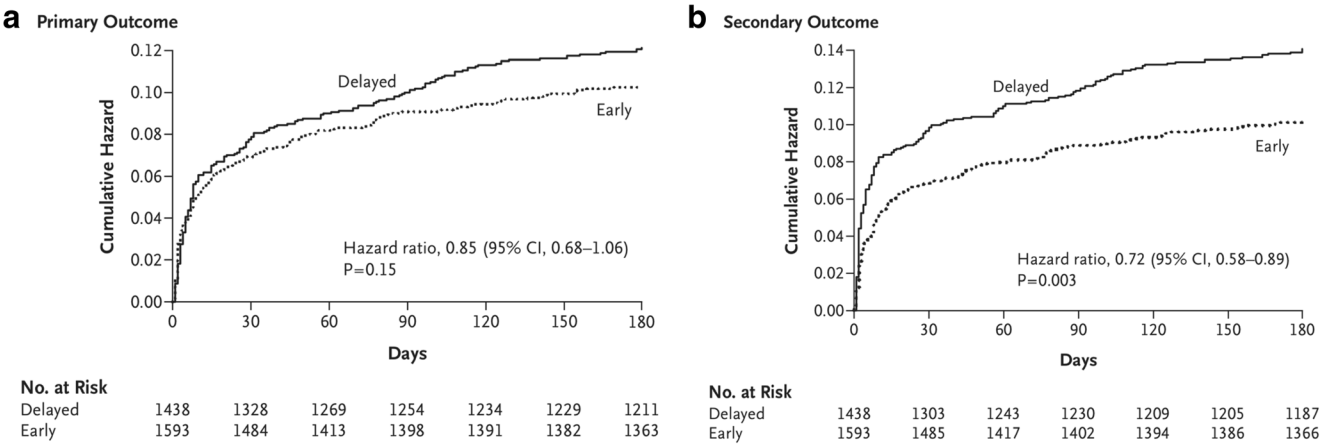

Fig. 1 Outcomes of early vs. delayed invasive approach to management of ACS patients in the TIMACS study. The difference in the composite primary outcome of death, myocardial infarction, or stroke in the early-intervention and delayed-intervention group did not reach statistical significance (panel **a**). However, early intervention was associated with strong and statistically significant reduction in the risk of the composite secondary outcome of death, myocardial infarction, or refractory ischemia, compared with the delayed intervention group (panel **b**). (From Mehta SR, et al. N Engl J Med. 2009;360(21):2165–75, Copyright © 2009 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society) [2]

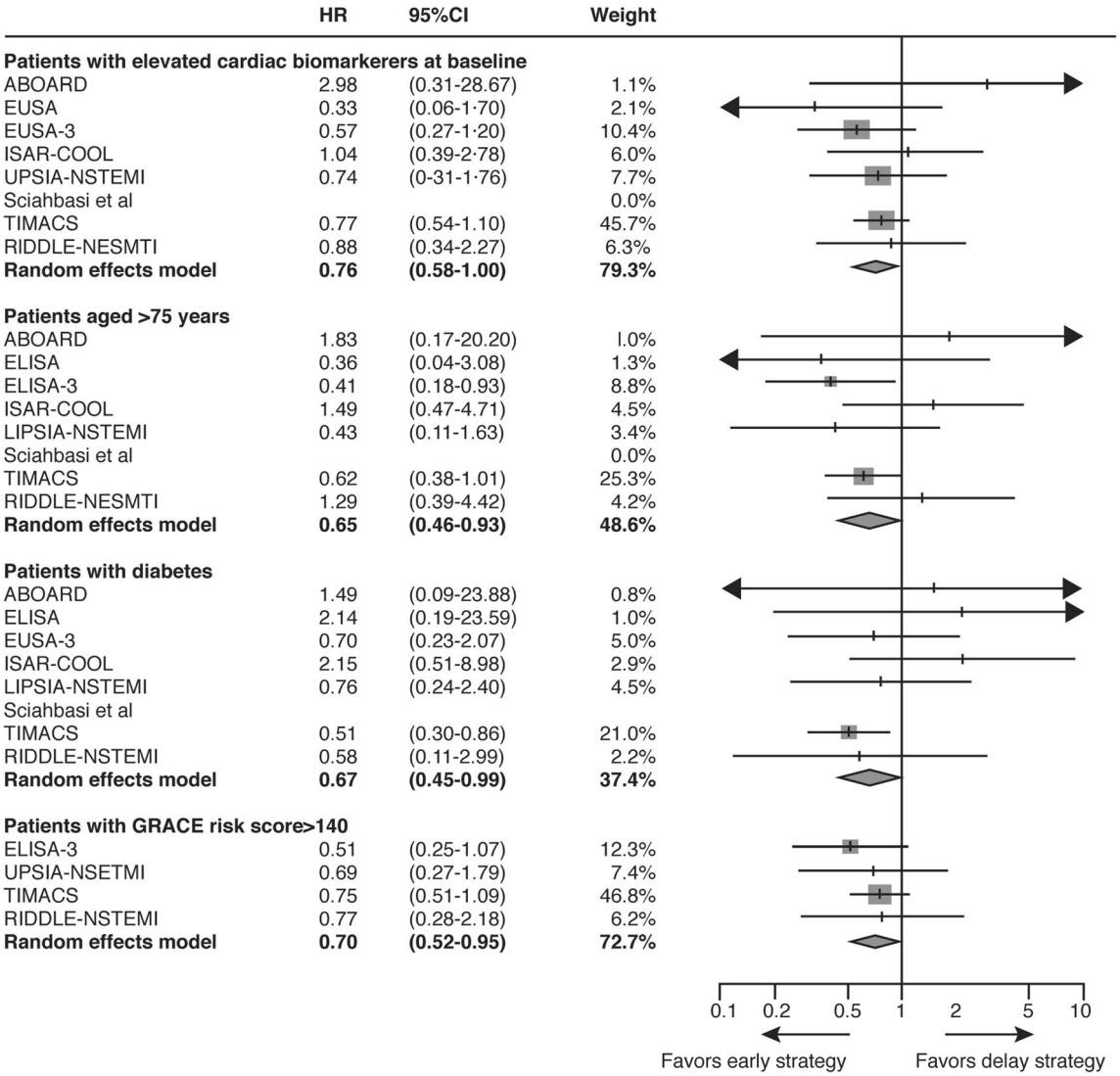

Fig. 2 Survival benefit of early invasive approach demonstrated in high-risk ACS patient subsets. In a meta-analysis of 5000 ACS patients enrolled in 8 randomized trials, an early invasive approach was not associated with survival benefit for all comers. However, survival benefit was statistically significant in pre-specified high-risk subgroups such as shown here (positive biomarkers, diabetes, elderly, high GRACE score). (Reprinted from *The Lancet*, Jobs A, et al. Lancet. 2017;390(10096):737–46, with permission from Elsevier) [17]

discussed in detail below. In patients eligible for either approach, long-term mortality is comparable with both strategies; however, rates of subsequent myocardial infarction and need for repeat revascularization are higher with PCI in most patient subsets with multivessel intervention [27, 28]. Patients who have concomitant valvular disease may be more appropriate for surgical correction, though a hybrid PCI/valve surgery management strategy is certainly a consideration. We will now focus on specific patient populations as well as general considerations regarding revascularization strategies.

Complete Vs Culprit-Only Revascularization

The incidence of multivessel CAD ranges from 29 to 60% [29, 30] and a crucial benefit afforded by CABG is the completeness of revascularization. Insights from the Bypass Angioplasty Revascularization Investigation (BARI) and the Arterial Revascularization Therapies Study demonstrated that incompletely revascularized patients tended to suffer from recurrent angina and need for repeat revascularization; this was largely driven by worse baseline clinical and angiographic characteristics [31, 32]. This conclusion is based on all-comers to the trials and information regarding how many NSTEMI patients were represented is unavailable. Multivessel PCI, however, has been shown to be safe in patients with NSTEMI, and patients treated with such an approach had similar rates of mortality and MI compared to those who underwent culprit-only PCI at 30 days and 6 months along with lower rates of repeated revascularization at 6 months of

follow-up [33]. It is challenging, however, to identify culprit lesions by angiography alone in patients with NSTEMI, and guideline documents are often lacking.

Several tools can be used to help guide the completeness of revascularization. The Synergy Between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery (SYNTAX) trial attempted to develop a more stratified approach for assessing revascularization options [34]. While it is a commonly employed tool for the interventionalist managing a patient with multivessel disease, its utility in the setting of NSTEMI is debatable as patients with acute myocardial infarction were excluded from the SYNTAX patient cohort. Another useful tool is fractional flow reserve (FFR) where deferred revascularization in lesions above a cutoff of 0.75 is associated with lower major adverse cardiovascular events [35]. Utilizing FFR in the setting of NSTEMI has been confirmed with similar predictive value [36]. Tools such as the SYNTAX score and FFR while helpful should again be used in light of the clinical judgment along with the risk versus benefit ratio always being considered.

If PCI is selected as the mode of revascularization, achieving complete revascularization in a single setting versus a staged fashion is a consideration. Conclusions from the Single-Staged Compared with Multi-Staged PCI in Multivessel NSTEMI Patients Trial (SMILE) supported one-stage over multistage revascularization in terms of reduced major adverse cardiac events. Although the staged procedures were completed within 7 days, the increased event rates in the staged PCI group were mainly attributable to an unexplained higher incidence of target vessel revascularization beyond the first 6 months [37]. As mentioned before, identifying culprit lesions in the setting of an NSTEMI with multivessel disease can be difficult and staging an intervention may lead to the possibility of performing the sentinel PCI on a non-culprit vessel. If complete revascularization can be achieved in a fashion that limits procedure time, exposure to high contrast volumes, and exposure to excess fluoroscopy, single-sitting PCI should be considered.

Diabetic Patients

Coronary artery disease is accelerated in diabetic patients as it is a pro-atherogenic condition due to increased endothelial dysfunction, more dyslipidemic states, increased platelet aggregation, and impaired fibrinolysis [38]. Roughly 25% of patients undergoing coronary revascularization have diabetes mellitus, though this percentage may be increasing in the last decade [39]. Regardless of the mode of revascularization, outcomes in diabetic patients are generally inferior to those in non-diabetics. Patients with diabetes undergoing CABG typically suffer from poor graft conduits and accelerated rates of venous bypass occlusion not to mention higher perioperative risks, while PCI outcomes are affected by high restenosis rates. The BARI trial sets the precedent demonstrating improved long-term survival with CABG [40]. These results were corroborated in the FREEDOM (Future Revascularization Evaluation in Patients with Diabetes Mellitus) trial which compared CABG with first-generation paclitaxel-eluting stents and the BEST (Randomized Comparison of Coronary Artery Bypass Surgery and Everolimus-Eluting Stent Implantation in the Treatment of Patients with Multivessel Coronary Artery Disease) trial which compared CABG to second-generation everolimus-eluting stents [41, 42•]. In a Canadian study examining the applicability of the FREEDOM trial data to the general population, about 5000 patients in a province-wide registry coronary revascularization (3047 PCI and 1802 CABG procedures) were followed for major cardiac and cerebrovascular events for 5 years. As expected, there was a significant advantage of CABG over PCI in reducing death and ischemic events. At 30 days, there was a significant interaction between the mode of revascularization and clinical presentation, with ACS patients benefiting from CABG much earlier than those presenting with stable disease (odds ratio for major events 0.49 [CI: 0.34 to 0.71]), whereas stable patients' event rates were not affected by revascularization strategy (odds ratio: 1.46 [CI 0.71 to 3.01]; p for interaction < 0.01). After 5 years, the advantage of CABG over PCI was almost equally noted in ACS and stable patients [43] (Fig. 3).

Despite the preponderance of evidence favoring CABG, the door for PCI is not completely closed in these patients as single and possibly double-vessel disease patients can benefit from PCI. Current antiplatelet therapies and aggressive secondary preventative strategies post-revascularization were not available or readily employed in previous studies.

Chronic Kidney Disease

Chronic kidney disease (CKD) represents a major independent risk factor for adverse outcomes in patients with acute coronary syndromes [10]. Patients with CKD, however, are more likely to be managed conservatively with revascularization reserved on for instances of recurrent myocardial ischemia. Furthermore, CKD patients are often excluded from major clinical trials making comparisons of PCI to CABG difficult to assess. Regardless of the mode of revascularization, outcomes in patients with CKD are less than ideal. In a patient undergoing CABG, CKD is an intrinsic adverse prognostic factor with markedly worse outcomes when compared to patients with normal renal function [44]. Patients with CKD undergoing PCI are affected by higher rates of restenosis on top of the ever-present risk of contrast-induced nephropathy [45, 46]. The only major randomized, prospective trial to assess differences between CABG and PCI in CAD patients with CKD was a subset of the ARTS trial. The two modes of revascularization demonstrated equivalent rates of death, MI, or stroke, though PCI was inferior with regard to reintervention rates; however, acute MI patients were excluded from the cohort [47].

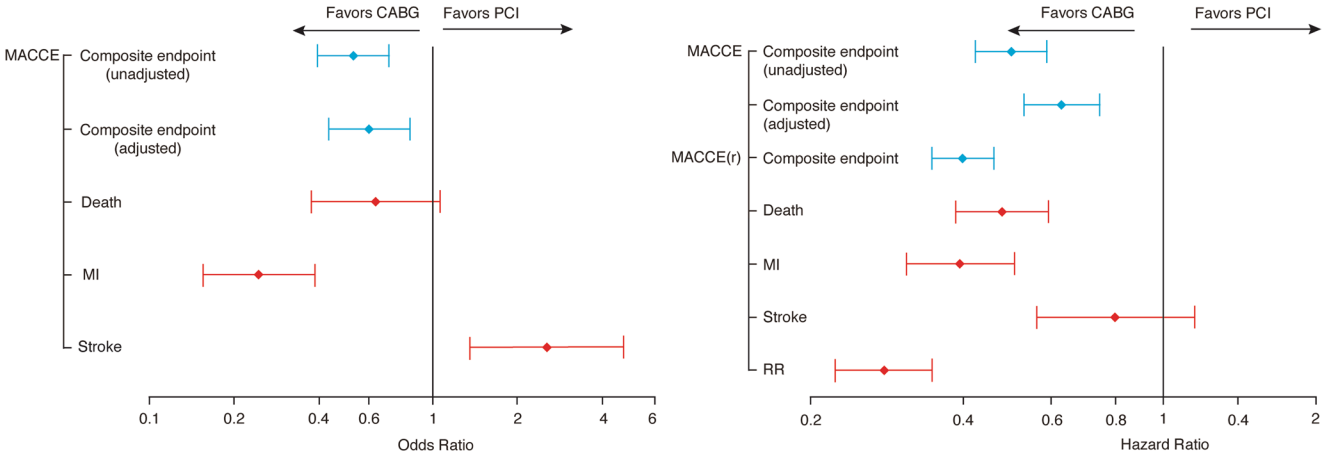

Fig. 3 Diabetics with ACS and multivessel disease in a real-life province-wide database. Left panel: The early impact of revascularization modality on the primary outcome (major adverse cardiac or cerebrovascular events, MACCE, a composite of all-cause death, nonfatal MI, and nonfatal stroke) and secondary outcomes (the individual components of MACCE) expressed as odds ratios (ORs). The ORs for primary outcome of MACCE were adjusted for age, sex, presentation (ACS vs. stable disease), urgency (emergent, urgent vs. elective), and LVEF (> 50%, 30–50% vs. < 30%). The ORs for MACCE (unadjusted and adjusted) as well as for each of the component outcomes (except for stroke) favored CABG over PCI as the revascularization mode of choice for these patients. Right panel: The late impact of revascularization modality on MACCE, its individual components, repeat revascularization post-discharge (RR), and a composite of MACCE plus RR [MACCE(r)] expressed as hazard ratios (HRs). The HRs for unadjusted and adjusted MACCE, RR, MACCE(r), and individual components of MACCE significantly favored CABG compared to PCI as a revascularization modality. (Reprinted from Ramanathan K, et al. J Am Coll Cardiol. 2017;70(24):2995–3006, with permission from Elsevier) [39]

Left Main Coronary Disease

Significant (greater than 50% narrowing) left main CAD is found in 4–6% of all patients who undergo coronary angiography, and 10.7–11.2% of left main PCIs are performed in the setting of NSTEMI [48, 49]. Standard of care for patients with significant unprotected left main coronary disease is CABG as it confers significant survival benefit on repeated studies [50–52]. This concept was further validated in the Nordic-Baltic-British Left Main Revascularization Study (NOBLE) in which 17–18% of the cohort represented patients with acute coronary syndromes (not STEMI) [53] Revascularization by CABG was shown to be superior to PCI even for left main stenosis with low-intermediate SYNTAX scores (< 32) though this was mainly driven by the need for repeat revascularization included in the composite outcome. Patients with NSTEMI represented 13.2% of the total cohort in the Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) trial which demonstrated the non-inferiority of second-generation DES to CABG based on a primary composite endpoint of all-cause mortality, MI, and stroke [54•]. Comparisons of CABG to PCI in these studies did not account for the even newer advancements in stent technology, procedural technique, and medical therapy including antithrombotic strategies. Furthermore, PCI should be considered in settings where surgery carries prohibitive risk including cardiogenic shock. Given the clinical equipoise presented with low-intermediate left main disease, patient preference along with the heart team approach should be a crucial influence towards decision-making.

Cardiogenic Shock

Cardiogenic shock is typically seen in the context of STEMI, which causes acute left ventricular dysfunction from continued cardiac myocyte ischemia and necrosis. Cardiogenic shock can complicate either a large STEMI or NSTEMI, and while mortality was traditionally thought to be similar between the two groups [55, 56], contemporary data demonstrates the short-term mortality of NSTEMI-related shock is higher [57]. The reason for comparable mortality rates is likely because NSTEMI patients are older with more comorbid conditions including previous MI, heart failure, renal dysfunction, and peripheral vascular disease. Though NSTEMI patients in shock are more likely to have recurrent ischemia, they are less likely to undergo coronary angiography [55]. Nearly two thirds of patients in the Global Use of Strategies To Open Occluded Coronary Arteries (GUSTO)-IIb trial who developed shock in the setting of NSTEMI had three-vessel disease. Only a small fraction of patients, however, received revascularization. Percutaneous coronary angioplasty was associated with improved mortality at 30 days whereas patients who underwent CABG had worse outcomes [56]. Extrapolating these findings in the approach to the current era of

revascularization should be cautioned as the advancement of technology and medical therapy has made significant strides.

Dual Antiplatelet Therapy

One of the major concerns cardiothoracic surgeons may have in performing CABG in patients with NSTEMI is the increased risk of bleeding, a result of the push towards upstream use of oral antiplatelet medications, namely $P2Y_{12}$ inhibitors. Aspirin confers only a modest increase in bleeding risk for CABG, and preoperative aspirin is known to reduce operative morbidity and mortality [58–61]. While current recommendations are to withhold $P2Y_{12}$ inhibitors from 5 to 7 days in patients undergoing elective surgery because of the known associated risks of bleeding and need for transfusion, the risk of bleeding and transfusion should be weighed against the risk of delaying surgery [8••]. Previous studies have shown that performing CABG on clopidogrel therapy increases the risk for transfusions but does not increase mortality or the rate of re-operation for bleeding [62].

Hybrid Revascularization

Hybrid coronary revascularization (HCR) combines the principal benefit of CABG (minimally invasive grafting of an internal mammary artery to the left anterior descending) with PCI of the remaining vessels. With this approach, the durability of an arterial bypass conduit is married with the decreased invasiveness of PCI. The most traditional approach to HCR involved minimally invasive direct coronary artery bypass of the left internal mammary artery (LIMA) to the left anterior descending (LAD) coronary artery followed by PCI to the non-LAD vessels, often in a staged fashion.

Performance of PCI prior to CABG allows surgery to be an adequate bailout in the event of sub-optimal PCI but also minimizes global ischemia during occlusion of the LAD for anastomosis. For NSTEMI, PCI of a culprit non-LAD vessel can be performed first, followed by surgical revascularization including the LAD at a time dictated by the patient's clinical variables. This approach, however, may require the surgeon to be comfortable with operating on dual antiplatelet therapy. The alternative approach, where PCI is performed following CABG of the LIMA to LAD, is appealing in the drug-eluting stent era as dual antiplatelet therapy (DAPT) can be continued long term. Furthermore, the assurance of a protected LAD may provide confidence for the interventionalist to tackle lesions that are more complex and potentially mitigate the need for adjunctive mechanical circulatory support. This approach for the surgeon does require deliberate avoidance of prolonged global myocardial ischemia from long pump runs as well as careful attention to hemodynamics. Simultaneous CABG and PCI in one setting within hybrid operating suites is another alternative allowing for immediate complete revascularization but requires collaborative efforts between the interventionalist and the surgeon balancing the need for antithrombotic management and minimizing the risk of perioperative bleeding.

The results of a prospective cohort, 11-center National Institutes of Health-funded study, were largely disappointing with no significant difference in the rate of major adverse cardiac events at 12 months [63]. Notably, myocardial infarction only represented subset of all patients. A randomized trial with long-term outcomes, the Hybrid Revascularization Observational Study, is currently comparing the effectiveness of multivessel PCI with HCR.

Considerations for PCI

If PCI is selected as the preferred revascularization strategy for a patient, the subtleties and nuances in procedure technique are numerous. Some approaches are worth reviewing including vascular access. Though the benefits of radial access have been highly touted, and adoption is increasing (10.9% in 2011 to 25.2% in 2014), only a quarter of overall PCIs in the USA were performed from a transradial approach [64]. This percentage has now exceeded 33% in the CathPCI Registry. Several factors are at play including a steeper learning curve, which can result in longer procedure times and greater radiation exposure. Interventionalists, however, should push for increased transradial access for PCI as it is associated with a similar rate of procedural success, reductions in the risk of bleeding and vascular complications, lower costs, and improved patient satisfaction, and improved mortality [65]. A recent meta-analysis pooling 22,843 patients across a spectrum of coronary artery disease found significant reductions in all-cause mortality for patients with NSTEMI on subgroup analysis [66].

Chronic total occlusions (CTO) are common in patients with NSTEMI and represent and independent predictor for mortality and reduction in left ventricular function [67]. The reason why concurrent CTOs may affect prognosis in NSTEMI patients may be in part related to the higher risk profile of CTO patients in general (older age, previous MI, reduced left ventricular function). In one study, the presence of a CTO in patients with NSTEMI independent from that of the infarct-related artery was associated with higher 30-day, 6-month, and 1-year mortality [68]. Notably in this study, the presence of a CTO did not affect the extent of either percutaneous or surgical coronary revascularization. The steep learning curve, technical difficulties, and lower procedural success for CTO PCI may favor complete revascularization via CABG in the correct clinical context.

Conclusion

Patients with NSTEMI represent a challenge for the cardiologist to individualize patient care and provide timely revascularization that will maximize benefit while minimizing exposure to harm. Risk assessment should be performed as soon as a diagnosis of NSTEMI is made with prompt decision-making regarding the need for invasive assessment of coronary anatomy. Recent evidence supports an early invasive approach in most patients, with evidence of reduced mortality and adverse ischemic outcomes in high-risk subsets. The decision to revascularize and the mode of revascularization should carefully integrate the patient's clinical characteristics as well as the complexity of the coronary anatomy.

Compliance with Ethical Standards

Conflict of Interest Bennet George, Naoki Misumida, and Khaled M. Ziada declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This review complies with all ethical standards for clinical research on human subjects. This article does not contain any studies with human or animal subjects performed by any of the authors.

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