

EDITORIAL

Managing Acute Coronary Syndromes in Older Adults With Chronic Kidney Disease: Are We There Yet?

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Acute coronary syndrome (ACS) remains among the leading causes of mortality worldwide. Older age and kidney dysfunction have been strongly associated with poor outcomes in patients with ACSs.^{1,2} The actuarial survival at 75 years in the United States is estimated to be 86.8 years, with some estimates predicting a 40% increase in population living beyond 80 years by the year 2040.³ Kidney dysfunction (estimated glomerular filtration rate [eGFR] <60 mL/min per 1.73 m²) increases with age, with an estimated prevalence of nearly 50% in adults >80 years of age.⁴ Although nearly a third of patients admitted with acute myocardial infarction (MI) and two thirds dying from MI are >75 years of age, <10% of patients in ACS trials reported are ≥75 years of age, with patients >85 years of age making up only 2% of trial populations.⁵ Current studies on the management of ACS in elderly patients are limited to small underpowered trials.^{6,7} Therefore, on the basis of the existing data, it is hard to draw robust conclusions about the management decisions in this complex group of patients. In this issue of the *Journal of the American Heart Association (JAHA)*, Holzmann and Siddiqui retrospectively compared outcomes in 12 821 patients >80 years of age with concomitant chronic kidney disease (CKD) presenting with non-ST-segment-elevation (NSTEMI) ACS and undergoing percutaneous coronary intervention (PCI) with their medically treated counterparts, using data from the SWEDEHEART (Swedish Web-System for Enhancement and Development of Evidence-Based

Care in Heart Disease Evaluated According to Recommended Therapies) registry.⁸ Given the relative paucity of data in this cohort, which is commonly encountered in clinical practice, these findings are both important and timely but need to be interpreted keeping the nonrandomized study design in mind.

See Article by Holzmann and Siddiqui

The 2014 American Heart Association/American College of Cardiology and the 2015 European Society of Cardiology guidelines for the management of patients with NSTEMI-ACS^{9,10} encouraged the consideration of an invasive strategy in elderly patients presenting with NSTEMI-ACS (class I and class IIa recommendations, respectively) while accounting for their comorbidities, frailty, life expectancy, and wishes. However, guideline recommendations do not always translate into clinical practice and are often delayed when they do. Holzmann and Siddiqui⁸ reported that coronary angiography during index hospitalization was performed in only 43% of patients, of whom nearly two thirds underwent PCI. In patients with eGFR 30 to 60 and 15 to <30 mL/min per 1.73 m², low rates of PCI were noted (22% and 10%, respectively).⁸ This “risk paradox” has also been seen in other registries, in which higher-risk patients are managed less intensively. Devlin et al reported a similar observation from

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GRACE (Global Registry of Acute Coronary Events), where only 33% of patients >80 years of age underwent coronary angiography and only 18% underwent PCI despite their high-risk status.¹¹ Similar observations were reported from the Australian national ACS registry, with 49% of patients >75 years of age undergoing coronary angiography (compared with 70% of patients <75 years of age).¹² In the CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the ACC/AHA [American College of Cardiology/American Heart Association] Guidelines) registry and Euroheart ACS survey, lower rates of coronary angiography and revascularization were noted in elderly patients.^{13,14} The proportions of patients undergoing coronary angiography and revascularization, reported by Holzmann and Siddiqui,⁸ are comparable to what has been observed in other registries and lend credence to their findings. The SWEDEHEART registry also builds on the existing knowledge base by bringing to light the important finding of low rates of revascularization in elderly patients with concomitant CKD, something that has not been specifically reported before. The appropriateness for not performing coronary angiography in individual patients is difficult to ascertain in SWEDEHEART registry, a registry of real-world practice. In general, registry patients tend to be sicker, with more comorbidities than those enrolled in clinical trials.¹⁵ The perceived bias on a lower chance of PCI success and higher complication rates in older adults exists, despite contemporary studies reporting a success rate comparable to that in younger population in elderly patients with acceptable complication rates.¹⁶ Therefore, this finding is of considerable importance as it highlights a disparity in health care and an opportunity for improvement.

In the current report, the authors noted a progressive increase in long-term mortality at a mean follow-up of 3.2 years as the eGFRs declined, from 42% in patients with eGFR >60 mL/min per 1.73 m² to 56% and 76% in patients with eGFR 30 to 60 and 15 to <30 mL/min per 1.73 m², respectively.⁸ This finding strengthens prior observations that elderly patients with worsening kidney function have worse outcomes after an ACS.^{17,18} On the other hand, there is a growing body of evidence suggesting that older patients derive a similar benefit with early revascularization in NSTEMI-ACS. These data have been derived from small underpowered studies in elderly patients, with minimal data on patients >80 years of age and CKD reported to date. In the current report, the investigators noted a lower adjusted risk of death in older patients associated with PCI compared with conservative management across all strata of eGFR.⁸ The reduction in mortality with PCI remained significant, with narrow CIs even after multivariable adjustment and propensity score matching (0.66 [0.55–0.79], 0.63 [0.54–0.74], and 0.54 [0.38–0.77] in

patients with eGFR >60, 30–60, and 15–<30 mL/min per 1.73 m², respectively). On the basis of their findings and the lack of other pertinent definite data, the investigators encourage physicians to consider PCI in this cohort.

Although the finding of lower mortality in elderly ACS patients with renal dysfunction who undergo PCI is intriguing, it must be interpreted with caution, keeping in mind the inherent limitations of the study, many of which were acknowledged by the authors themselves. First and foremost, this is a retrospective observational analysis, in which many unmeasured and unaccounted variables and baseline factors may confound the observed relationships despite laudable efforts at elaborate multivariable and propensity score matching adjustment. For example, the authors included both type 1 and type 2 MIs as part of their population, but did not report the exact proportion of these patients in each treatment cohort. This may have influenced the treatment strategy as patients undergoing PCI may have had a higher rate of true type 1 MIs than those who did not undergo PCI. Of note, patients with type 2 MI usually have worse prognosis compared with their type 1 MI counterparts. The benefits of an invasive strategy among patients with type 2 MI are also not well established. Moreover, patients undergoing PCI had a lower incidence of clinical heart failure, which could have influenced the findings. There are also no data on patients' frailty, which is an important, independent marker of adverse events in elderly patients with ACS.¹⁹ The investigators also did not report or adjust for baseline risk scores (eg, Thrombolysis in Myocardial Infarction [TIMI] or GRACE risk scores), which incorporate baseline variables not captured in SWEDEHEART registry and which are both independent and powerful predictors of outcomes in patients with NSTEMI-ACS. Notably, the lack of statistically significant reduction in MI in favor of PCI demands a careful review as nearly all prior high-quality data uniformly demonstrated a lower incidence of recurrent MI in patients who undergo PCI, which is considered the most consistent end point driving the salubrious benefits of invasive strategy after NSTEMI-ACS.²⁰ In the current study, rates of recurrent MI during admission were higher across all strata of eGFRs in the PCI group, and it is also unclear whether investigators were able to adequately discern between periprocedural MI and recurrent spontaneous MI, which portend different clinical implications. This raises questions about the study conclusions and the possibility of a selection bias related to the healthy subject effect. Finally, Holzmann and Siddiqui reported no statistically significant increase in rates of life-threatening bleeding in all cohorts, except patients with eGFR 15 to <30 mL/min per 1.73 m².⁸ However, before fully adapting the results of this study as evidence of safety of PCI in octogenarians with CKD, data on thrombotic strokes

and worsening renal function, especially rates of hemodialysis, should be also examined.

So, how would the current report influence the care of elderly ACS patients with CKD who present with NSTEMI-ACS in our practice? On the basis of the current study and prior evidence, older age and presence of CKD alone should not preclude revascularization, as many of these appropriately selected patients tend to benefit from an invasive strategy. However, other important factors, like cognitive impairment, comorbidities, frailty, and patient wishes, should be factored in. A multifaceted heart team approach, similar to what has been adopted for patients considered for transcatheter aortic valve replacement procedures, is reasonable and should include not only a clinical and an interventional cardiologist but possibly the patient's primary care physician and a geriatrician.

ARTICLE INFORMATION

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Disclosures

None.

REFERENCES

- Lopes RD, Gharacholou SM, Holmes DN, Thomas L, Wang TY, Roe MT, Peterson ED, Alexander KP. Cumulative incidence of death and rehospitalization among the elderly in the first year after NSTEMI. *Am J Med*. 2015;128:582–590.
- Soveri I, Arnlov J, Berglund L, Lind L, Fellstrom B, Sundstrom J. Kidney function and discrimination of cardiovascular risk in middle-aged men. *J Intern Med*. 2009;266:406.
- Schneider EL. Aging in the third millennium. *Science*. 1999;283:796–797.
- Grams ME, Chow EK, Segev DL, Coresh J. Lifetime incidence of CKD stages 3–5 in the United States. *Am J Kidney Dis*. 2013;62:245–252.
- Alexander KP, Newby LK, Armstrong PW, Cannon CP, Gibler WB, Rich MW, Van de Werf F, White HD, Weaver WD, Naylor MD, et al. Acute coronary care in the elderly, part II: ST-segment elevation myocardial infarction: a scientific statement for healthcare professionals from the American Heart Association Council on Clinical Cardiology: in collaboration with the Society of Geriatric Cardiology. *Circulation*. 2007;115:2570–2589.
- Savonitto S, Cavallini C, Petronio AS, Murena E, Antonicelli R, Sacco A, Steffenino G, Bonechi F, Mossuti E, Manari A, et al. Early aggressive versus initially conservative treatment in elderly patients with non-ST-segment elevation acute coronary syndrome: a randomized controlled trial. *JACC Cardiovasc Interv*. 2012;9:906–916.
- Tegn N, Abdelnoor M, Aaberge L, Endresen K, Smith P, Aakhus S, Gjertsen E, Dahl-Hofseth O, Ranhoff AH, Gullestad L, et al. Invasive versus conservative strategy in patients aged 80 years or older with non-ST-elevation myocardial infarction or unstable angina pectoris (After Eighty study): an open-label randomised controlled trial. *Lancet*. 2016;387:1057–1065.
- Holzmann MJ, Siddiqui AJ. Outcome of percutaneous coronary intervention during non-ST-segment-elevation myocardial infarction in elderly patients with chronic kidney disease. *J Am Heart Assoc*. 2020;9:e015084. DOI: 10.1161/JAHA.119.015084.
- Amsterdam EA, Wenger NK, Brindis RG, Casey DE, Ganiats TG, Holmes DR, Jaffe AS, Jneid H, Kelly RF, Kontos MC, et al. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes. *J Am Coll Cardiol*. 2014;64:e139–e228.
- 2015 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur Heart J*. 2016;37:267–315.
- Devlin G, Gore JM, Elliott J, Wijesinghe N, Eagle KA, Avezum A, Huang W, Brieger D. Management and 6-month outcomes in elderly and very elderly patients with high-risk non-ST-elevation acute coronary syndromes: the Global Registry of Acute Coronary Events. *Eur Heart J*. 2008;29:1275–1282.
- Malkin CJ, Prakash R, Chew DP. The impact of increased age on outcome from a strategy of early invasive management and revascularisation in patients with acute coronary syndromes: retrospective analysis study from the ACACIA registry. *BMJ Open*. 2012;2:e000540.
- Skolnick AH, Alexander KP, Chen AY, Roe MT, Pollack CV Jr, Ohman EM, Rumsfeld JS, Gibler WB, Peterson ED, Cohen DJ. Characteristics, management, and outcomes of 5,557 patients age \geq 90 years with acute coronary syndromes: results from the CRUSADE initiative. *J Am Coll Cardiol*. 2007;49:1790–1797.
- Rosengren A, Wallentin L, Simoons-Smit AM, Gitt AK, Behar S, Battler A, Hasdai D. Age, clinical presentation, and outcome of acute coronary syndromes in the Euroheart acute coronary syndrome survey. *Eur Heart J*. 2006;27:789–795.
- Steg PG, Lopez-Sendon J, Lopez de Sa E, Goodman SG, Gore JM, Anderson FA Jr, Himbert D, Allegro J, Van de Werf F. External validity of clinical trials in acute myocardial infarction. *Arch Intern Med*. 2007;167:68–73.
- Summaria F, Romagnoli E, De Luca L, Mustilli M, Pagnanelli A. Feasibility and safety of transradial approach and bivalirudin treatment in elderly patients undergoing early invasive strategy for ACS: “The OLDER Research Project” preliminary study. *J Cardiovasc Med (Hagerstown)*. 2012;13:351–352.
- Bhatia S, Arora S, Bhatia SM, Al-Hijji M, Reddy YNV, Patel P, Rihal CS, Gersh BJ, Deshmukh A. Non-ST-segment-elevation myocardial infarction among patients with chronic kidney disease: a propensity score-matched comparison of percutaneous coronary intervention versus conservative management. *J Am Heart Assoc*. 2018;7:e007920. DOI: 10.1161/JAHA.117.007920.
- Szummer K, Lundman P, Jacobson SH, Schön S, Lindbäck J, Steneström U, Wallentin L, Jernberg T; SWEDEHEART. Influence of renal function on the effects of early revascularization in non-ST-elevation myocardial infarction: data from the Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies (SWEDEHEART). *Circulation*. 2009;120:851–858.
- Duo Q, Wang W, Wang H, Ma Y, Hai S, Lin X, Liu Y, Zhang X, Wu J, Dong B. Prognostic value of frailty in elderly patients with acute coronary syndrome: a systematic review and meta-analysis. *BMC Geriatr*. 2019;19:222.
- Fox KA, Clayton TC, Damman P, Pocock SJ, de Winter RJ, Tijssen JG, Lagerqvist B, Wallentin L; FIR Collaboration. Long-term outcome of a routine versus selective invasive strategy in patients with non-ST-segment elevation acute coronary syndrome: a meta-analysis of individual patient data. *J Am Coll Cardiol*. 2010;55:2435–2445.