International Journal of Geriatrics and Gerontology

OPEN ACCESS

Gasperetti CM. Int J Geriatr Gerontol 6: 135.

www.doi.org/10.29011/2577-0748.100035

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Research Article

Variations in the Treatment of Coronary Syndromes in Nonagenarians

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Citation: Gasperetti CM (2022) Variations in the Treatment of Coronary Syndromes in Nonagenarians. Int J Geriatr Gerontol 6: 135. DOI: 10.29011/2577-0748.100035

Received Date: 27 August, 2022; **Accepted Date:** 24 September, 2022; **Published Date:** 28 September, 2022

Abstract

Recent studies have examined the results of treatment of nonagenarians with percutaneous coronary intervention (PCI) and found promising survival benefits for patients treated with PCI. Despite these benefits, there continue to be large variations in patient selected for PCI based on such factors as frailty, gender, chronic disease, and age. These factors and other patient presentations form the basis for wide variation in treatment and underscore that future studies may increase understanding of patient selection and predict nonagenarians who benefit most from treatment.

Keywords: Nonagenarian; Octogenarian; Gender; Frailty; Acute coronary syndrome; ST elevation Myocardial infarction; PCI and Survival

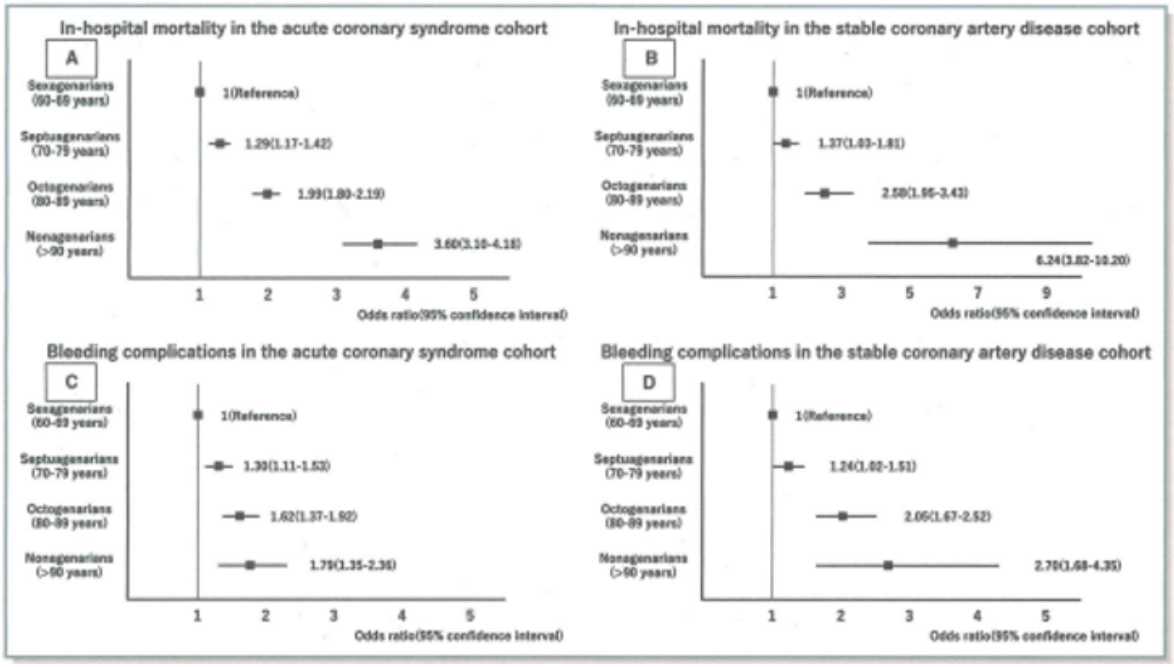
To Treat Nonagenarians?

Nonagenarians who present to the hospital with coronary syndromes present a unique dilemma for patients and physicians alike. Treating such patients encourages one to revisit the adage of "do no harm". Yet nonagenarians who present with coronary syndromes may actually be helped by decisions to perform PCI. Importantly, age itself varies with the patient as a patient's chronological age may not represent a patient's physical age. Frailty also may exist in part due to fear of ambulation as it can stimulate further cardiac symptoms. These are important factors for discussion with patients and families who ultimately need to be able to make educated decisions.

Recent publications include studies of outcomes in nonagenarians with both unstable and stable syndromes. Previously, many clinical studies excluded such patients due to their age and gender. Exclusion may continue to be difficult, however, as the population of nonagenarians continues to grow. In 2020, the number of nonagenarians had grown to 2.1 million in the US (30 million worldwide). In the US, the population is predominantly female by 2:1. Currently it is expected that women will have a life expectancy of 90 years by 2030. Following is a review of recent publications which include comparisons of nonagenarians vs. octogenarians, comparisons of gender in nonagenarians, and outcomes with use of PCI vs. medical therapy in patients who present with coronary syndromes. Risks inherent in the process of selection and treatment are also reviewed.

Comparison of Nonagenarians with Patients Greater than 60 Years of Age (Sexagenarians), 70 years of Age (Septuagenarians), 80 Years of Age (Octogenarians)

Numasawa Y, et al. using a prospective registry, compared outcomes in PCI in the elderly and contrasted the results in patients greater than 60, 70, 80, and 90 years [1]. This study was an observational national study performed in Japan which included 562,640 patients ≥ to 60 years of age hospitalized between 2014 and 2016. Of these patients, there were 6,780 nonagenarians with acute coronary syndromes (53.9% STEMI of 6,780) and 3,848 nonagenarians with stable coronary artery disease (60.5% of 3,848). ACS and in particular STEMI patients are known to be at high risk and in comparison to other patients from 60 years to 89 years in the group, nonagenarians had higher death rates for in hospital mortality for both unstable syndromes (5.2%) and stable syndromes (0.6%) and more bleeding complications (1.1% vs. 0.6%, respectively) (Figure 1). Nonagenarians also had greater comorbidities, Chronic Kidney Disease (CKD), frailty, and cognitive impairment. They were also more likely to present with cardiogenic shock. Importantly, the authors also found that the use of radial artery access was an inverse independent predictor for both in hospital mortality and bleeding. Indeed, it is currently state of the art for STEMI intervention and circumvents the complication of bleeding which occurs with femoral access.



Adjusted odds ratios for in-hospital mortality and bleeding complications in each age group. Separate multivariable logistic regression analysis was performed for in-hospital mortality and bleeding complications in each cohort. Adjusted models include age, female sex, history of heart failure, acute heart failure, presentation or diagnosis, cardiogenic shock, diabetes mellitus, chronic kidney disease, 3-vessel disease, left main trunk lesion, and access site in the acute coronary syndrome cohort (**A** and **C**); and age, female sex, history of heart failure, diabetes mellitus, chronic kidney disease, 3-vessel disease, left main trunk lesion, and access site in the stable coronary artery disease cohort (**B** and **D**).

Figure 1: Adjusted odds ratios for in-hospital mortality and bleeding complications in each age group [1].

Bruno RR, et al. studied nonagenarians versus octogenarians admitted 3 (Clinical Trials.gov) of Very old ICU Patients (VIP) [2]. Of 7900 patients included, 10% were nonagenarians. Age, gender, frailty, organ failure, and ICU mortality were examined. Withholding or withdrawing treatment was also recorded. Nonagenarians had higher rates of frailty but less acute organ dysfunction than octogenarians. Nonagenarians had an increased risk for withholding life sustaining therapy 35% vs. 27%, but not withdrawing it (13% v. 14%). They received significantly less mechanical ventilation 41% vs. 52%, renal replacement therapy 4% vs. 11%, and vasoactive drugs 52% vs. 59%. Mortality was similar at ICU discharge (27% vs. 27%). The authors noted that after adjustment for multiple relevant confounders, nonagenarians did not suffer from worse outcomes compared to octogenarian ICU patients. Long term results were not yet available at the time of publication. The authors stress that triage decisions should be according to severity of illness and functional capacity, and not age.

Comparison between Genders among Nonagenarians with Acute Coronary Syndromes

Cepas-Guillen PL, et al. using a retrospective review compared sex based differences in ACS management in a group of patients over 90 years of age [3]. Consecutive patients were studied at four academic centers in Spain. A total of 680 patients were included of which 55% had non STEMI and 45% had STEMI. There were more women than men in each group as shown below (Figure 2) and less women than men underwent PCI for treatment. Men had a higher disease burden, more peripheral arterial disease (PAD), chronic obstructive lung disease (COPD), active oncologic disorder, and prior MI. Women were found to be more frail and with higher disability and cognitive impairment. Women were also found to be less likely to undergo PCI mainly in the STEMI group (45% vs. 60%, p = .01). An important finding was that the mortality rate was similar between groups of women and of men both in hospital (18% vs. 16%, p= .4) and at one year follow up (37% vs. 41%, p= .3 respectively). When patients treated with PCI were compared to those treated with medical therapy alone, no differences were found in use of radial access, TIMI flow post procedure, or medical therapy at discharge. However, the survival rate was better for those treated with PCI vs medical therapy and the survival benefit at one year was higher in women vs. men who had PCI (82% vs. 68%, p =.008) (Figure 3). Independent predictors of not undergoing STEMI were age, disability, and female gender.

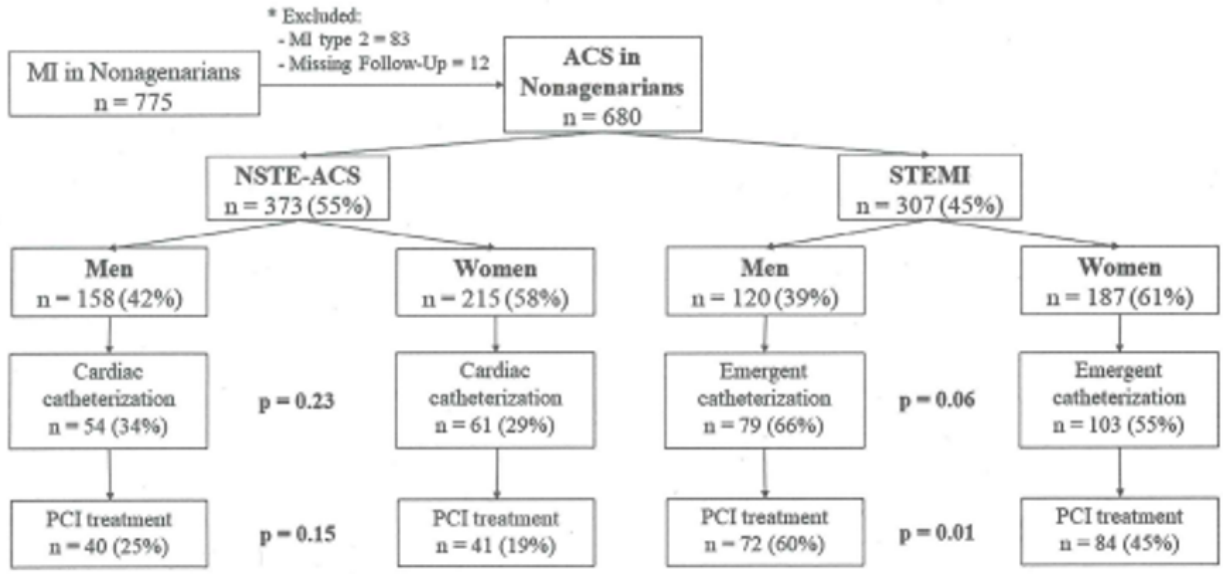


Figure 2: From 2005 to 2018, 680 nonagenarian patients with Acute Coronary Syndrome (ACS) were included. MI: Myocardial Infraction; STEMI: ST-elevation Myocardial Infraction; NSTE-ACS: non-ST-elevation acute coronary syndrome; PCI: Percutaneous coronary intervention [3].

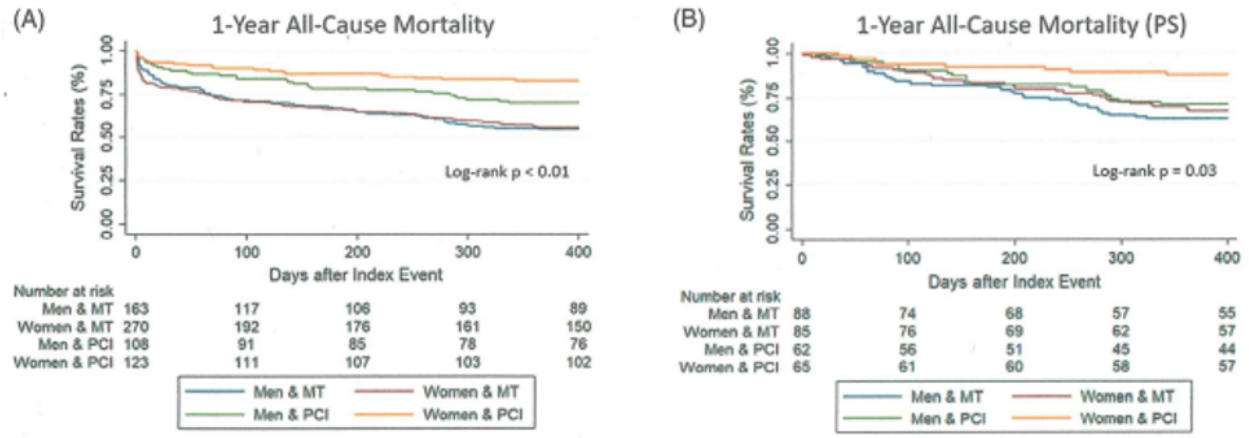


Figure 3: Kaplan-Meier survival estimated for 1-year-All-Cause Death. Legend by sex and treatment: 1 year survival rates: All cohort (A) and propensity-matching scores cohort (B). PCI: Primary Percutaneous Coronary Intervention; MT: Medical Treatment; PS: Propensity-matching Score [3].

The authors summarize several studies in their discussion which corroborate their findings, including a study by Sulzgruber P, et al. [4] which found that women of > 80 years with ACS benefited more from PCI than men and have lower mortality than men. A study from China by Hao Y, et al. [5] also showed that women were less likely to receive evidence-based treatment including early dual antiplatelet therapy, heparin, and reperfusion therapy than men. Some of this bias is seen due to atypical presentations and also occurs in young women. When the presentation is clear, i.e. STEMI, for example, guidelines recommend immediate PCI for STEMI care, regardless of age and gender. A higher burden of frailty is also felt to influence physicians to not offer PCI. However, women at any age have a higher frailty index although their life expectancy is felt to be longer, a phenomenon termed the “morbidity-mortality paradox”.

Comparison of Nonagenarians Treated with Primary PCI (PPCI) for Acute Myocardial Infarction vs. Nonagenarians Treated Medically

Recent publications from 2020-2022 address the treatment of acute ST Elevation MI including clinical outcomes, management of ST elevation MI, and comparison to those patients treated medically. Meah, et al. performed a retrospective single center study examining nonagenarians who presented to a tertiary center between 2013 and 2018 [6]. Typical STEMI criteria were used to identify STEMI patients: symptoms of myocardial ischemia > 30 minutes, new ST-segment elevation, new left bundle branch block or paced rhythm. Complete infarct was defined as symptom onset >12 hours prior to admission. For all patients radial access was employed.

111 patients were studied (STEMI in 98 (88.3%) and NSTEMI in 13 (11.7%). PPCI was performed in 42 patients (37.8%), while 69 patients (62.2%) were treated with medical management. More patients with a history of atrial fibrillation were managed medically 16 (23.2%) vs. 1 patient with atrial fibrillation (2.4%) treated with PPCI. More patients who were managed medically had completed infarcts on presentation: 30 patients (43.5%) than did those with treatment with PPCI: 2 patients (4.8%). Findings revealed a trend towards increased 30-day mortality in the medically managed vs. the PPCI group (40.6% vs. 23.8% p=0.07). At three-year follow-up, however, a statistically significant difference in survival was noted which favored the PPCI group (48.1% vs. 21.7%) vs. the medically managed group (Figure 4). Importantly, when the patients in the medically managed group were removed from the analysis, the survival benefit continued for those receiving PPCI (44.3% vs. 14.6%, p = 0.01). The authors concluded that patients who underwent PCI on presentation with STEMI had a lower mortality rate than those who were treated with medical therapy.

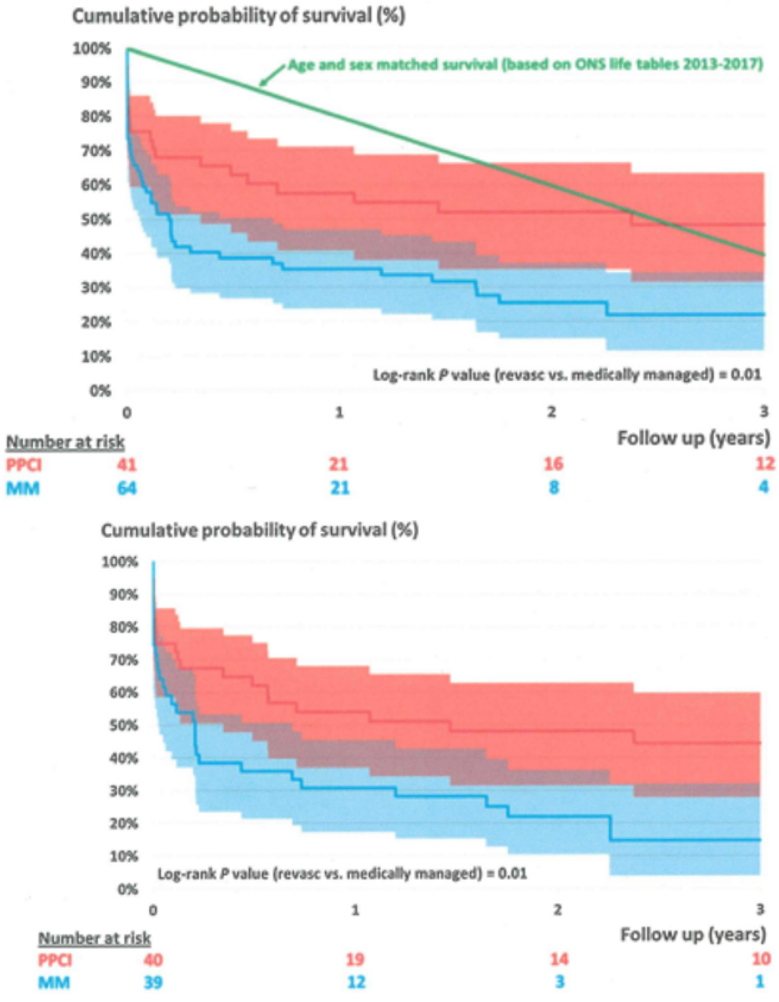


Figure 4: (A) Kaplan Meier for all-cause mortality. (B) Kaplan Meier for all-cause mortality excluding completed infarcts [6].

Nishihira K, et al. studied 96 nonagenarians who presented with acute MI and underwent PCI [7]. PCI success rate was 83.3%. In hospital major bleeding was 15.6% and in hospital mortality was 17.7%. Mortality at one year was 27.5%. Mortality was higher for patients who had balloon pump placement, cardiogenic shock, and final TIMI flow <3 and lower for patients who had cardiac rehabilitation in hospital after their procedures. For patients post PCI, 40% were considered frail on presentation to hospital. There was also an increase in frailty in patients following PCI (Figure 5).

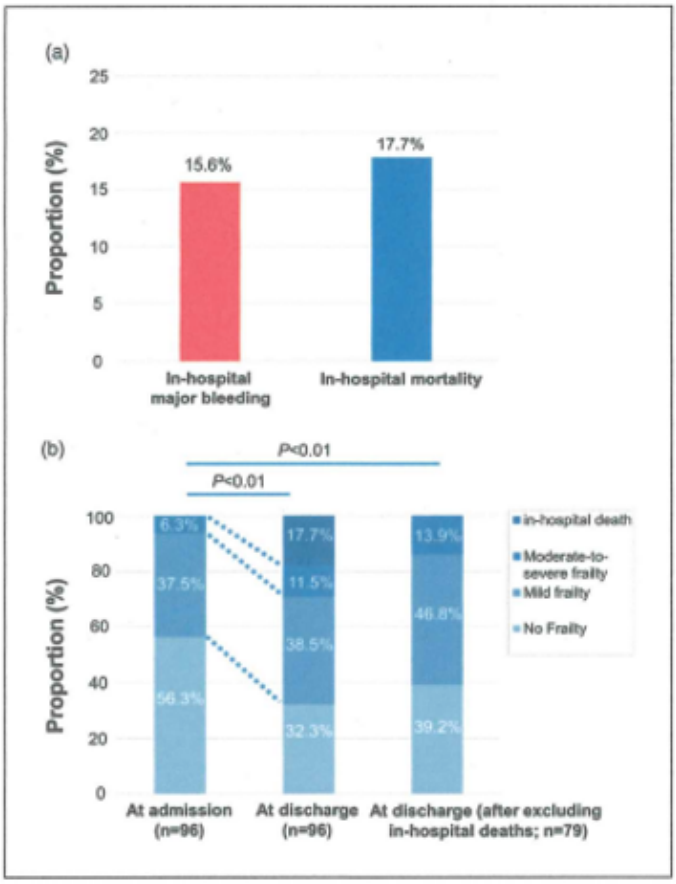


Figure 5: (a) In-hospital major bleeding rate and In-hospital mortality. (b) Change in frailty status during hospitalization [7].

Lee J, et al. in a retrospective study analyzed 41 nonagenarians with acute MI (both STEMI and NSTEMI) between 2006 and 2015 [7]. 24 (59%) were treated with PCI and 17 (41%) were treated with medical therapy. Both 30-day and one-year mortality were lower in the PCI group than in the medical treatment group (17% vs. 65%, p < 0.001 [30-day mortality]) and 21% vs. 76%. p < 0.001 [one-year mortality], respectively. This finding persisted even excluding patients in the medical group that presented with Killip 4 and for subgroup analyses, showing that PCI patients were 3 x more likely to have survived (Figures 6 and 7).

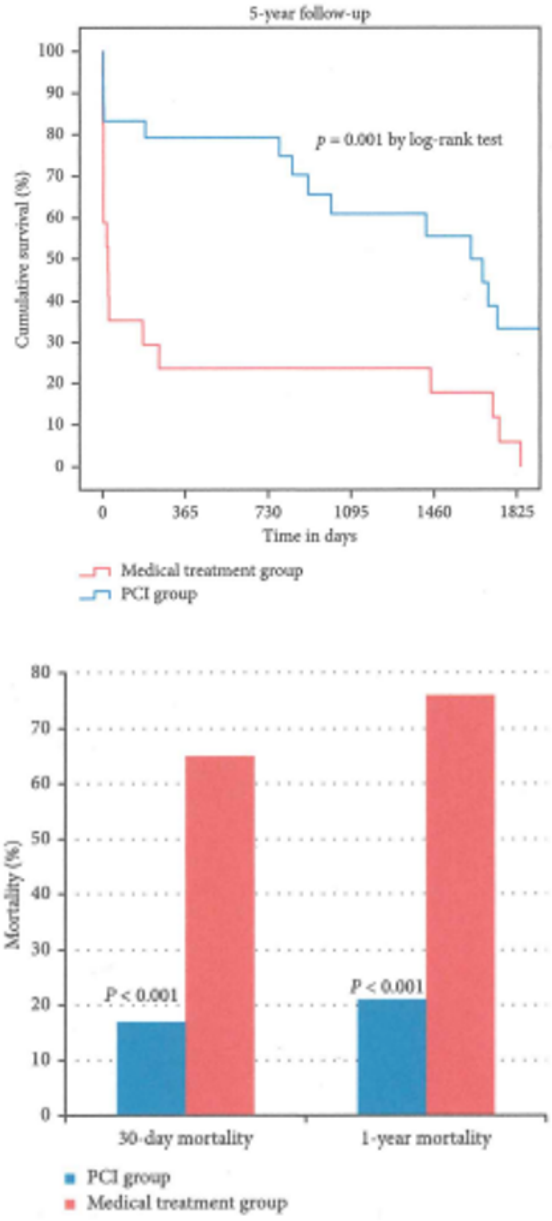


Figure 6: (a) Kaplan-Meier curves of survival in the PCI group and medical treatment group. (b) Thirty-day and one year mortality rates of the PCI group and medical treatment group [8].

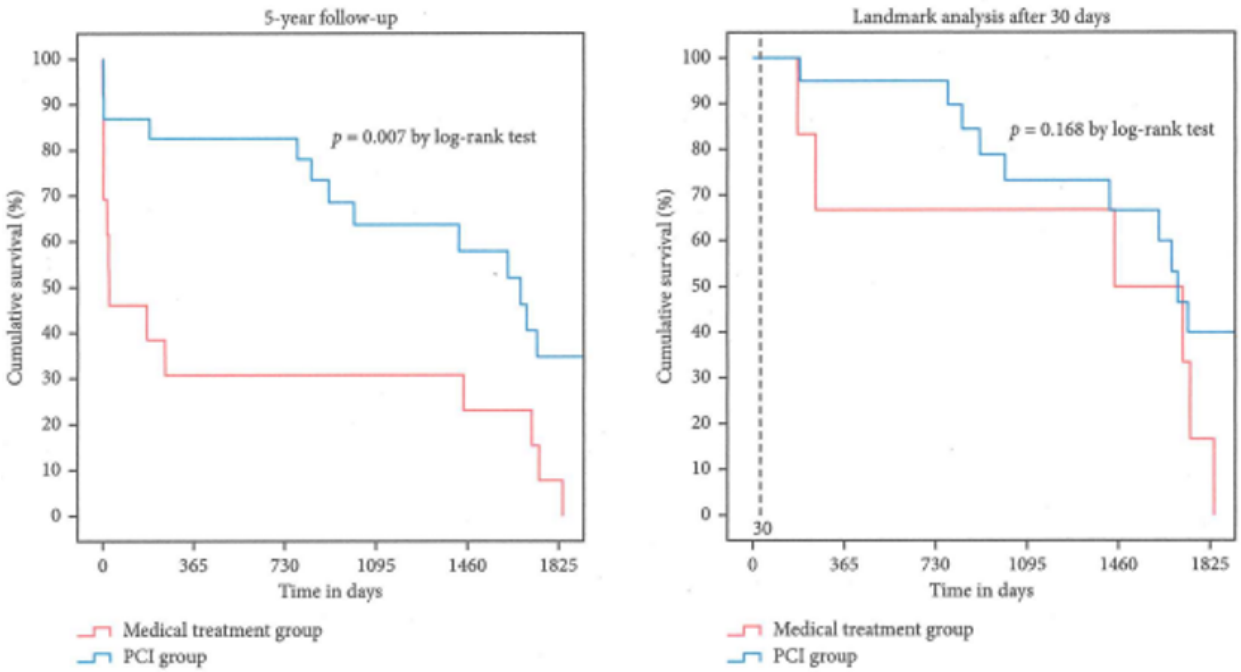


Figure 7: (a) Kaplan-Meier curves of survival in the PCI group and medical treatment group, excluding Killip class 4 patients. (b) Kaplan-Meier curves of survival in the PCI group and medical treatment group after 30 days [8].

Seok Oh, et al. studied 1,467 consecutive nonagenarians drawn from Korean AMI registries from 2005 to 2200 and compared those who had PCI and those who did not [9]. The primary endpoint was 1 year Major Adverse Cardiac Events (MACE) including all cause death, non-fatal myocardial infarction, and any revascularization. Findings were that the all cause death and 1-year MACE was higher in the non-PCI group. After reviewing the study and correcting for any confounding variables the conclusions were that nonagenarians with acute MI have better clinical outcomes, receive more optimal medical therapy, and receive high quality PCI.

Risk Factors for Nonagenarians Undergoing PCI

In summary, several studies have found that treatment with PCI in nonagenarians after presentation with acute coronary syndromes and acute MI confers a survival benefit. There are many variations in the use of PCI for nonagenarians, however. These studies reveal a wide range of use or nonuse of PCI in patients with acute syndromes sometimes from 0 to 100%. Reasons given against treating with PCI in acute syndromes included presence of atrial fibrillation without anticoagulation, completed MI on presentation, patients with high Killip score and more severe illness, patients in cardiogenic shock, and frailty. Gender was also found to be a factor, with women excluded from PCI in some studies despite demonstrating higher and longer term benefit when they undergo PCI. As summarized by Zoccai GB, et al. the decision to proceed with PCI relies on the likelihood of procedural success, ischemic/thrombotic risk, and risk of bleeding [10]. Unfortunately, the longer the wait to intervene with ST elevation MI, the higher the mortality and the greater the missed opportunity.

Among the factors which increase the safety and success in the use of PCI in this elderly population are radial access with very low rate of bleeding at the access site, intravascular ultrasound and flow reserve which offer higher precision, the use of "lithotripsy" for treating coronary calcium making it easier to stent calcified lesions. These advances have made calcification, tortuosity, and complex disease more tenable. In addition, smaller catheters and sheaths, including sheathless access, better understanding of anesthetic risk in patients of advanced age, and availability of rehabilitation for patients with initial frailty help to address critical issues found in nonagenarians. Evaluating initial patient status in order to care for these patients is also difficult as nonagenarians may have different declines related to cognition or physical ability. Indeed, many older patients perform better in their own home environment than in the hospital setting, and particularly during myocardial infarction. As the aging population continues to grow, large clinical trials must consider broadening their criteria to include nonagenarians and thus open the door for understanding differences in treating nonagenarians and the decisions made for their treatment.

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