

Comorbidities and Complications in Nonagenarians Undergoing Coronary Angiography and Intervention

Tertiary Center Analysis

Mohamed GAYED,¹ MD, Nour YADAK,², Waad QAMHIA,², Yunis DARALAMMOURI,², and Marc-Alexander OHLOW,³

SUMMARY

Elderly people represent the fastest growing portion of cardiovascular patients. We aimed to analyze the clinical presentation, risk factors, co-morbidities, complications, and mortality in patients 90 years or more who underwent coronary angiography and intervention.

We retrospectively studied 108 (0.25% of 43,385) consecutive patients ≥ 90 years undergoing cardiac catheterization and/or intervention in a tertiary specialist hospital between 2003 and 2014.

Most patients (68.5%) were introduced on an emergency basis, especially with acute coronary syndrome (ACS) (63.8%). Non-STEMI accounted for two-thirds of the myocardial infarctions. We found higher prevalences of previous coronary artery disease (CAD) (38%), other atherosclerotic diseases (20.4%), cardiac risk factors such as hypertension (84.3%), diabetes (49.1%), hyperlipidemia (50.9%), heart failure (42.6%), atrial fibrillation (AF) (25.0%), severe aortic stenosis (13.0%), severe mitral regurgitation (3.7%), and implantable devices (25.0%), and co-morbidities such as renal impairment (48.1%), COPD (12.0%), and previous stroke (6.5%). Three-vessel disease was present in 34.6% of the patients. The left anterior descending artery (LAD) was the most affected coronary artery (67.6%). Percutaneous coronary intervention (PCI), mostly with bare metal stents (BMS), was used to manage 54.6% of the patients, and it failed in 4 of the patients. Conservative treatment was used in 39.8% of the patients and 15.7% had no significant CAD.

The incidences of vascular complications, such as bleeding (6.5%), bleeding in other organs (6.5%), blood transfusion (6.5%), in-hospital paroxysmal atrial fibrillation (7.4%), in-hospital successful reanimation (2.8%), complete heart block (5.6%), acute renal impairment (23.1%), associated infection (25.9%), cardiogenic shock (14.8%), and death (15.7%) were high.

Considering the more extensive risk factors, CAD and co-morbidities, acute presentation and age per se, we believe that the reported higher rates of complications and mortality are still acceptable. (Int Heart J 2017; 58: 180-184)

Key words: Elderly, Coronary artery disease, Cardiac catheterization

During the past several years, demographic data have been showing an increase in the number of elderly, which is most predominant in Western countries, and it is expected to increase even further. In the United States, studies have shown that the number of people older than 80 years was 9.3 million in 2000. This number is predicted to double (19.5 million) by 2030 and triple by 2050.¹⁾ In Germany, the percentage of people older than 80 years was 5.3% (4.3 million) in 2010 and the number of people older than 100 years is doubling every 8 years.^{2,3)}

This increase in age is associated with increased prevalences of hypertension, diabetes, CAD, and other chronic illnesses. Cardiovascular diseases are still the leading cause of death in Europe, accounting for 47% of deaths.⁴⁾

The increasing prevalence, consequences, morbidity, and

mortality of CAD warrant aggressive prevention and management measures. PCI is an established method of treatment for chronic and acute CAD.⁵⁾

Despite these trends, there are limited data on the efficacy and safety of PCI in very elderly patients. The bulk of the clinical evidence and experience relies, however, on relatively young patients. Furthermore, patient case-mix has varied substantially between the studies in elderly, and as a result, PCI outcomes in octogenarians have varied widely in the published data. For example, the mortality rate ranged from 0% to 34%.⁶⁻⁸⁾

The aim of this retrospective study was to analyze the clinical presentation, risk factors, co-morbidities, complications, and mortality in patients 90 years or older who underwent coronary angiography and PCI at our center between

From the ¹ MVZ am Küchwald GmbH, Chemnitz, Germany, ² An-Najah National University, West Bank, Palestine, and ³ Department of Cardiology, Zentralklinik Bad Berka, Bad Berka, Germany.

Address for correspondence: Mohamed Gayed, MD, MVZ am Küchwald GmbH, 1 Klinikum Oberberg/Kreisklinikum Waldbröl, Dr-Goldenbogen-Straße 10, 51545 Waldbröl, Germany. E-mail: moha_ragab2003@yahoo.com

Received for publication February 15, 2016. Revised and accepted May 30, 2016.

Released in advance online on J-STAGE March 21, 2017.

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2003 and 2014.

METHODS

Study population: Our study was conducted in a retrospective method. The data used were collected using the database of the Zentralklinik Bad Berka for all patients who underwent diagnostic coronary angiography or intervention between 2003 and 2014. In this period, a total of 108 nonagenarians out of 43,385 consecutive patients undergoing cardiac catheterization or PCI were included in our study. Oral/written consent was obtained from all patients who underwent cardiac catheterization. There were no exclusion criteria.

The following parameters were assessed: 1) Clinical presentation. 2) Patient related factors: age, gender, arterial hypertension, diabetes mellitus, hyperlipidemia, smoking, family history of CAD, previous myocardial infarction, previous PCI, previous coronary artery bypass graft (CABG), heart failure, cardiogenic shock (defined as systolic pressure < 90 mmHg for at least 30 minutes), peripheral artery disease (PAD), AF, and ejection fraction (EF). 3) Comorbidities: chronic renal impairment (CRI), chronic obstructive pulmonary disease (COPD), anemia (hemoglobin (Hb) less than 7 mmol/L), and infection. 4) Procedure related factors: number of diseased epicardial arteries, type of treatment (PCI versus CABG versus medical therapy), and emergency procedures. 5) Complications: vascular complications (eg, large groin hematoma or entry-site bleeding with significant fall of Hb (Hb fall ≥ 2.5 mmol/L), pseudo-aneurysm and arterio-venous fistula), major blood loss (defined as bleeding associated with significant fall of Hb (Hb fall ≥ 2.5 mmol/L), eg, gastrointestinal bleeding), contrast induced acute renal failure (CIARF) (defined as oliguria or anuria with increase in serum creatinine > 0.5 mg/dL, or $> 50\%$ from baseline creatinine or the need for hemodialysis at any time after the procedure), peri-procedural myocardial infarction (defined as troponin increase more than 5 times the upper limit of normal), acute stent thrombosis (defined as stent thrombosis < 24 hours after stent implantation), subacute stent thrombosis (defined as stent thrombosis > 24 hours to 30 days after stent implantation), and in-hospital mortality (defined as death in the catheterization lab or during the post procedural hospital stay), and cerebrovascular accident (CVA) defined as a permanent loss of neurologic function (including coma) caused by an ischemic vascular event. 6) Death: both cardiac and all causes mortality.

Coronary angiography was interpreted visually on site by each operator. Percutaneous coronary revascularization procedures were performed using conventional methods at the discretion of the operator.

Statistical analysis: For continuous variables, we used the mean \pm standard deviation, where frequencies were measured for categorical variables. Differences between groups were analyzed using the Fischer exact test for categorical variables. A probability value of $P < 0.05$ was considered to be statistically significant.

RESULTS

General: From 2003 to 2014, 108 nonagenarians out of

43,385 (0.25%) patients underwent diagnostic coronary angiography or intervention at our tertiary hospital. The mean age was 92.1 ± 2.0 years and 55 patients (50.9%) were males.

Clinical presentation: Most nonagenarian patients, 74 (68.5%), were introduced on an emergency basis with one patient (0.9%) due to resuscitation for unclear cause. Among these 108 patients, 69 (63.8%) presented with ACS (including 9 (8.3%) with unstable angina (UA), 36 (33.3%) with non-ST-elevation myocardial infarction (NSTEMI), and 24 (22.2%) with ST-elevation myocardial infarction (STEMI)). Before admission, two patients with STEMI developed ventricular fibrillation (VF) and were resuscitated successfully. One of these 2 patients developed acute pulmonary edema (APE). Four patients (3.7%) presented with APE due to hypertensive crisis. Eight out of 24 patients with STEMI arrived within 12 hours from the onset of symptoms (33.3%). Approximately one-third (34) of the patients (31.5%) presented electively. Eight patients (7.4%) had stable angina despite medical treatment and a high probability of CAD. Five patients (4.6%) presented with heart failure with reduced EF $\leq 45\%$. Seven patients (6.5%) presented with cardiac arrhythmias (mainly AF and multiple risk factors for CAD) and 14 (12.9%) with symptomatic valvular heart disease (mainly severe aortic stenosis) (Supplemental Figure 1).

Atherosclerosis and risk factors: Almost all nonagenarians had arterial hypertension, about half had diabetes and hyperlipidemia, and about one in 4 had previous myocardial infarction or other atherosclerotic vessel disease (Supplemental Figure 2).

Cardiac status and co-morbidity: The mean blood pressure at admission was 142.0 ± 27.4 mmHg systolic and 79.2 ± 13.5 mmHg diastolic. The mean heart rate was 85.2 ± 29.6 and the mean EF was 47.6 ± 15.5 .

The prevalences of heart failure, AF, valve disease, and implantable devices were high. About half of the patients had renal impairment, although none were on dialysis (Supplemental Table I). One patient (0.9%) had dementia. Medications at the time of admission are presented in Supplemental Table II.

Results of angiography: Coronary angiography and intervention were performed via the radial approach in 29.6% of the patients. Four cases had to be switched to a femoral artery access. As a consequence, the femoral access was used in a total of 80 patients (74.1%).

Three-vessel disease (3VD) was present in 34% of the patients. LAD was the most affected artery. Two of 5 patients with previous CABG had undergone one bypass graft. PCI with mostly bare metal stents was used to manage 54.6% of the patients, 4 of whom experienced failure due to unsuitable anatomy of the vessels. Conservative treatment was used in 39.8% of the patients and 15.7% had no significant CAD (Supplemental Table III).

Adjuvant therapy with glycoprotein 2b3a was used in 5.2% of the patients, 3.7% had received intra-aortic balloon pumping, and 3.7% had a pulmonary catheter due to cardiogenic shock.

Complications:

Vascular and bleeding complications The incidences of vascular complications and bleeding in other organs other than at the puncture site were both 6.5%. A significant fall in hemoglobin was observed in 9.3% and 6.5% received a blood transfusion (Supplemental Table IV).

Cardiac complications and arrhythmia Among the 108 patients, two (1.6%) had peri- interventional infarction, one (0.9%) re-infarction due to acute in-stent thrombosis, and 3 (2.8%) pulmonary edema. One patient (0.9%) had pericardial effusion which was treated conservatively, and only one patient (0.9%) had thrombus in the left ventricle due to a left ventricular aneurysm.

During the hospital stay, one patient (0.9%) was successfully resuscitated due to developed asystole. Six patients (5.6%) developed complete atrioventricular block and they were treated using temporary pacemakers. Also, one patient (0.9%) developed ventricular fibrillation and was successfully resuscitated. One patient developed iatrogenic ventricular fibrillation (during left ventricle wiring) and was successfully defibrillated and resuscitated. Eight patients developed paroxysmal AF. Finally, one patient (0.9%) developed atrial tachycardia.

Variable complications Among the complications, 28 patients (25.9%) had infection (17.6% had pneumonia and 8.3% had urinary tract infection (UTI)), 5.6% had post interventional delirium, 0.9% had an allergic reaction due to contrast media, and 23.1% had CIARF (Supplemental Table V).

Shock and death The incidence of shock in our cohort was 17 patients (15.7%). One of these 17 (5.9%) had septic shock. The majority (15/17, 88.2%) were cardiogenic due to pump failure, and one (5.9%) was due to ventricular septal defect due to myocardial infarction.

The mortality rate was 15.7% (17 patients out of 108). Of these, 9 (52.9%) died due to cardiogenic shock as a result of pump failure. The mortality in nonagenarians in cardiogenic shock was 9/15 (60%). One patient (5.9%) died due to cardiogenic shock due to VSD and 3 patients (17.6%) due to complete heart block and asystole. One patient (5.9%) died due to acute renal failure. Two patients (11.8%) died due to multiple organ failure. One patient (5.9%) was admitted due to out-of-hospital cardiac arrest. Acute ischemia by coronary angiography could be excluded and the patient died of an unknown cause.

DISCUSSION

The most important findings in our cohort of 108 nonagenarians were 1) the high incidences of cardiovascular risk factors and co-morbidities and therefore the peri-interventional complications, shock and mortality, 2) The high rate of associated infection, and 3) Lack of enthusiasm for performing a diagnostic or interventional procedure in this population that is growing in number.

Basic characteristics and clinical presentation: In contrary to many studies that reported higher proportions of males⁹⁻¹¹ or females,¹² we found no gender predominance in our study.

In accordance with other studies, nonagenarians in our study underwent coronary angiography almost on an emergency basis, especially with the diagnosis of ACS, reflecting the skepticism about the efficacy and safety of elective invasive procedures in the very elderly, the decreased frequencies of symptomatic CAD in men and women by age 80, the increasing silent ischemia, and the atypical presentation.^{3,5,7} Also, the high rate of patients that were treated conservatively despite the presence of relevant CAD in our study (25.9%) reflects and

confirms this skepticism, and perhaps explains the worry of bleeding complications under dual antiplatelet drugs the higher use of BMS than DES in our study.

In our study, we found that non-STEMI accounts for two-thirds of the myocardial infarctions in this elderly population. This agrees with the results of Schwartz, *et al.*⁵ As expected and reported in other studies, due to atypical presentation, most patients with STEMI arrived more than 12 hours after the onset of symptoms.^{13,14}

As in previous to other studies,^{7,15-19} nonagenarians in our study had substantially higher prevalence and severity of atherosclerotic CAD with increasing prevalence of triple- vessel CAD, cardiac risk factors such as hypertension and diabetes, decreased EF, arrhythmia and especially atrial fibrillation, number of patients with implantable devices, valvular heart disease, and comorbidities, particularly CRI. In contrast with other studies, the prevalence of hyperlipidemia in our study was high. However, the prevalence of obesity was significantly lower among patients older than 90 years. This is a common finding in very old populations and is mainly due to malnutrition.^{20,21}

Complications and outcome: The reported rates of vascular and bleeding complications, peri-interventional infarction, and cerebrovascular stroke were comparable with the percentages described by Batchelor, *et al.*⁷

The frequency of CIARF is approximately 13% in non-diabetics and 20% in diabetics undergoing elective PCI.²² Among these patients, the consequences of dialysis is relatively rare (0.5-2%), but the in-hospital mortality rate was high at 36%.²³ In our study, we reported collectively a relatively higher rate of CIARF (23%). In this group, only one patient (4%) had to be dialized, but unfortunately they later died.

Although the infection complication rate of cardiac catheterization is zero,²⁴ and this theme is nowadays irrelevant, we have reported a very high rate of associated infections (25.9%). About two-thirds of the patients had a lower respiratory tract infection and one-third had a urinary tract infection. This can be explained by deceased immunity with age, malnutrition, decreased mobility, the high rate of associated diseases such as DM, COPD, and renal impairment, and higher rates of complications that require a prolonged hospital stay. We believe that this issue is important and must be investigated in greater detail.

We reported a high incidence of life-threatening bradyarrhythmia and tachyarrhythmia that were managed adequately and timely as well as a high incidence of shock mainly due to pump failure.

Previous results of clinical studies regarding death rate were highly variable, ranging from no early deaths up to rates as high as 34%.²⁵⁻²⁹ Several studies demonstrated a continuous, curvilinear manner of mortality after elective coronary angiography and/or coronary intervention with increasing age, ranging from about 0.5% for patients < 55 years old to about 5% for patients > 85 years old.⁷ This difference may be even more pronounced in the setting of acute coronary syndrome.^{13,30,31}

Batchelor, *et al* determined 7 independent predictors of mortality for octogenarians undergoing coronary interventions including increased age, cardiogenic shock, acute myocardial infarction, left ventricular systolic function, renal insufficiency, first coronary angioplasty, and diabetes mellitus.^{7,32-34} In their study, “Older” octogenarians (age > 85 years) had a two-fold

risk for mortality compared to octogenarians < 85 years old.⁷ Additionally, anemia per se was associated with higher in-hospital mortality and poor long-term outcome in patients presenting with STEMI undergoing primary PCI.^{35,36}

Because of the high prevalence of these predictors in our study the mortality rate in our study was high (15.7%). This is higher than in the national cardiovascular collaboration network or the French registry which reported a short-term mortality of 3.8% and 3.4%, respectively.^{7,37} However, the coronary angiography and interventions in both studies were elective. Also, this rate was higher than that reported in the Euro Heart Survey on coronary revascularization (8%). However, this survey was conducted on relatively younger patients (patients older than 75 years with STEMI treated by PCI).³⁸ Our result was comparable to the results of a study from the Myocardial Infarction Registry (MIR) with more than 8000 octogenarians (mean age, 84 years) on in-hospital mortality following primary PCI (14%)¹⁷ and in the work of Zoccali, *et al* reporting a mortality of 14%.⁶

Was the coronary angiography and intervention in nonagenarians helpful?: In our study, we observed no statistically significant difference in the in-hospital mortality rate in patients who presented with ACS and were managed interventionally compared to those who were managed conservatively.

However, by comparing the in-hospital mortality rate in the subgroup of patients who presented with STEMI and were successfully managed by intervention with those patients who were treated conservatively and those not successfully managed interventionally, the in-hospital mortality rate was found to be significantly lower ($P = 0.02$) in those who were successfully managed by intervention. Similarly, Renilla, *et al* and Hirakawa, *et al* found that the morbidity rate was higher among elderly patients (> 85 years and > 80 years old, respectively) with STEMI treated conservatively than in patients who were treated interventionally.^{39,40} In the Belgian STEMI registry, the in-hospital mortality rate in haemodynamically stable octogenarians who presented with STEMI and were treated interventionally was lower than that of the group treated conservatively.⁴¹

Limitations: The limitations of our study include the lack of a control group, and no group that was younger than 90 years and no group without coronary angiography that was intentionally treated in a conservative manner. The lack of follow-up is another limitation.

Conclusion: Considering the more extensive risk factors, CAD and co-morbidities, acute presentation, and age per se, we believe that the reported higher rates of complications and mortality are still acceptable, especially regarding the well-established role of coronary intervention in the management of acute myocardial infarction.

We recommend the use of safer techniques that are readily available, such as the radial approach to minimize vascular complications. Since this group of patients is expanding, we need to develop new materials such as smaller catheters and sheaths, and medications as antiplatelets and anticoagulants and contrast medium to prevent or at least reduce the expected complications of coronary intervention.

DISCLOSURE

Conflict of interest statement: On behalf of all authors, the corresponding author states that there is no conflict of interest.

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SUPPLEMENTAL FILES

Supplemental Table I, II, III, IV, V

Supplemental Figure 1, 2

Please see supplemental files;

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