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Original Article

Long-term clinical outcomes of patients with rheumatoid arthritis and concomitant coronary artery disease

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Abstract: Background: Rheumatoid arthritis (RA) is associated with high morbidity and mortality predominately due to increased cardiovascular risk. Few reports are available regarding the management of coronary artery disease (CAD) in RA patients and the long-term clinical outcomes after coronary revascularization. Methods and results: All consecutive patients with RA were identified by retrospective review at a rheumatology tertiary center in Milan, Italy between 2001 and 2013. RA patients affected by significant CAD (RA-CAD+) were prospectively followed for major adverse cardiovascular and cerebrovascular events (MACCE) after percutaneous coronary revascularization (RA-PCI), coronary artery bypass grafting (RA-CABG) or medical therapy (RA-MT). Among 936 patients with RA, the presence of clinically significant CAD was found in 5.6% (53 patients, RA-CAD+). Of these, 32 patients (60%) underwent PCI (RA-PCI), 10 patients (19%) underwent CABG (RA-CABG) and 11 patients (21%) treated with MT (RA-MT). After a mean follow-up of 9±7 years, the rate of MACCE was 56% in RA-PCI patients, 50% in RA-CABG and 27% in RA-MT patients (P=0.184). The high MACCE rate was mainly driven by repeat coronary revascularization (47%) in the RA-PCI group and high rate of strokes (30%) in RA-CABG patients. Conclusion: In patients with rheumatoid arthritis and concomitant coronary artery disease (RA-CAD+), we observed at long-term follow-up a high MACCE rate, predominantly in those who underwent coronary revascularization.

Keywords: Coronary artery disease, percutaneous coronary intervention, coronary artery bypass grafting, rheumatoid arthritis

Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by inflammatory arthritis, joint destruction and disability. In 2013, the United States Center for Disease Control and Prevention for Rheumatoid arthritis reported an overall 0.5-1% prevalence, with a female to male ratio of 2:1, with higher incidences occurring from the fifth decade onwards. RA is associated with high morbidity, including physical and work-related disability and increased mortality, predominantly due to accelerated coronary artery and cerebrovascular disease [1]. Indeed, cardiovascular (CV) events occur approximately a decade earlier in RA patients [2], suggesting that RA, like diabetes mellitus, is a risk factor for premature CV disease [3]. The increased CV risk in RA appears to be due to both chronic inflammation and traditional risk factors [4, 5].

Besides the increased risk of developing CV disease, there are additional factors occurring more frequently in RA patients that may worsen the clinical outcome of RA patients with a concomitant coronary artery disease (CAD), including an increased frequency of diffuse multivessel coronary artery disease, microvascular coronary artery disease [6] and a disparity in the quality of care [7].

Despite the high-risk profile of RA patients, only a few data are available regarding long-term

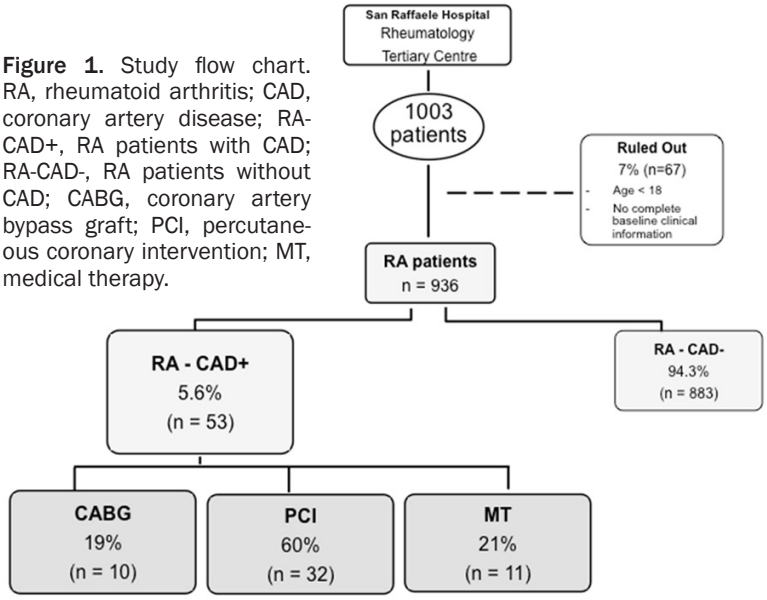

Figure 1. Study flow chart. RA, rheumatoid arthritis; CAD, coronary artery disease; RA-CAD+, RA patients with CAD; RA-CAD-, RA patients without CAD; CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention; MT, medical therapy.

clinical outcomes during medical anti-ischemic therapy (MT) or after coronary revascularization including percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG). All this leads to uncertainty when choosing the best possible strategy for CAD management in this population.

In the present study, we aimed to evaluate long-term clinical outcomes after PCI, CABG or a prolonged period of MT in a real-world cohort of patients affected by rheumatoid arthritis (RA) and concomitant coronary artery disease (CAD).

Methods

Study design and population

We retrospectively identified all consecutive patients that were evaluated and prospectively followed at a rheumatological tertiary Italian center between 2001 and 2013 (San Raffaele Hospital, Milan, Italy). RA patients were defined eligible for the study if they had: (a) a diagnosis of RA confirmed by a rheumatologist according to the American College of Rheumatology criteria/European League Against Rheumatism [8]; (b) were ≥18 years of age and (c) had complete baseline clinical information available.

Clinically significant CAD was defined as the presence of symptomatic myocardial ischemia or evidence of inducible myocardial ischemia (demonstrated either by stress echocardiography or nuclear medicine stress test imaging) and concomitant evidence of significant coronary stenosis (>70%) at coronary angiography or coronary computed tomography angiography. Demographic information, lifestyle factors, duration and severity of RA, coronary procedural treatment, drug therapy, clinical and biochemical features of the metabolic syndrome and other characteristics were collected. All information was obtained through detailed electronic medical records review and from interventional cardiology and internal medicine databases. Other clinical data for baseline characteristics and those for clinical long-term follow-up were obtained through structured interviews, self-report questionnaires, physical examinations, and laboratory tests. Height (m) and weight (kg) were recorded at the time of coronary revascularization in order to calculate body mass index (BMI).

Disease Activity Score 28 (DAS28) was calculated by a rheumatologist in all patients at every ambulatory follow-up visit. DAS28 is a quantitative combined index to measure the disease activity in patients with RA largely used in daily clinical practice and clinical trials. The DAS28 combines information from 28 joints taking into account the number of swollen joints, the number of tender joints, erythrocyte sedimentation rate or C-reactive protein and the patient's self-report of general health.

All patients with RA and clinically significant CAD were stratified into three subgroups according to the management strategy followed: RA-PCI, RA-CABG, RA-MT (**Figure 1**).

Follow-up information on a patient's status if they missed appointments was obtained by telephone contact with either the patient, or with one of his or her immediate relatives and complemented by information obtained by patient charts from other hospital admissions. Written informed consent, approved by the Institutional Ethics Committee, was obtained

Table 1. Clinical characteristics of patients with rheumatoid arthritis with coronary artery disease (RA-CAD+) stratified into 3 sub-groups of therapeutic management: percutaneous/surgical coronary revascularization (RA-PCI/RA-CABG) and medical therapy (MT)

Clinical Characteristics	RA-CAD+ (n=53)	RA-PCI (n=32)	RA-CABG (n=10)	RA-MT (n=11)	*P* value
Age (years), mean ± SD	74.4±9.1	64±9.7	77±7	75.9±9.8	<0.001
Male gender; n (%)	28 (53)	21 (66)	6 (60)	1 (9)	0.004
Hypertension; n (%)	40 (75.5)	23 (72)	9 (90)	8 (73)	0.494
Dyslipidemia; n (%)	25 (47)	13 (41)	7 (70)	5 (45)	0.265
Smoker; n (%)	23 (43)	15 (47)	5 (50)	3 (27)	0.472
Diabetes mellitus; n (%)	12 (22.5)	10 (31)	1 (10)	1 (9)	0.18
Peripheral vascular disease; n (%)	8 (15)	5 (16)	2 (20)	1 (9)	0.777
Chronic renal failure*; n (%)	2 (4)	1 (3)	0 (0)	1 (9)	0.525
BMI, Mean ± SD	25±3	25±3	25±2	23.4±3.4	0.28
LVEF%; Mean ± SD	55±6.8	56±7	52±7	57.1±2.8	0.154
Disease Activity Score 28 (DAS28); Mean ± SD	4.8±1.3	4.92±1.72	5±1.2	4.2±0.9	0.352
Medical Therapy					
DMARDs; n (%)	47 (88.5)	28 (87.5)	28 (87.5)	9 (82)	0.399
Methotrexate	33 (62)	17 (53)	7 (70)	9 (82)	0.200
Leflunomide	4 (7.5)	2 (6)	2 (20)	0 (0)	0.202
Hydroxychloroquine	8 (15)	3 (9)	1 (10)	4 (36)	0.721
Chloroquine	4 (7.5)	2 (6)	2 (20)	0 (0)	0 (0)
Steroid therapy; n (%)	32 (60)	16 (50)	8 (80)	8 (73)	0.153
Biological agents; n (%)	7 (13)	3 (9)	2 (20)	2 (18)	0.591
Abatacept	2 (3.5)	1 (3)	1 (10)	0 (0)	0.463
Etanercept	5 (9.5)	2 (6)	1 (10)	2 (18)	0.504
Acetylsalicylic acid; n (%)	42 (79)	26 (81)	8 (80)	8 (73)	0.830
Clopidogrel; n (%)	9 (17)	9 (17)	0 (0)	0 (0)	0.281
Ticlopidine; n (%)	7 (13)	2 (6)	2 (20)	3 (27)	0.161
Prasugrel/Ticagrelor; n (%)	3 (5.5)	3 (9)	0 (0)	0 (0)	0.352
Warfarin; n (%)	4 (7.5)	1 (3)	2 (20)	1 (9)	0.071
Statin; n (%)	31 (58.5)	18 (56)	6 (60)	7 (64)	0.340
ACE-I/Sartan; n (%)	29 (55)	20 (62)	4 (40)	5 (45.5)	0.361
Calcium-antagonists; n (%)	18 (34)	10 (31)	2 (20)	6 (54)	0.217
Beta-blockers; n (%)	36 (68)	24 (75)	4 (40)	8 (73)	0.109
Other Antianginals (%)	15 (28)	4 (12.5)	1 (10)	7 (64)	0.001

Data are presented as absolute numbers and percentages, for categorical variables, or mean value ± SD, for continuous variables. *Chronic renal failure was defined as an estimated glomerular filtration rate <60 ml/min/1.73 m^2. Disease-Modifying Anti-Rheumatic Drugs (DMARDs), angiotensin-converting-enzyme inhibitor (ACE-I).

from all participants for the procedure, data collection and subsequent analysis and publication.

Study measures and endpoints definitions

The primary study endpoint was the rate of *Major Adverse Cardiac and Cerebrovascular Events* (*MACCE*: composite end-point of all-cause mortality, ischemic or hemorrhagic stroke, myocardial infarction, repeat revascularization); the secondary endpoint was the rate of *repeat revascularization* (TLR, TVR or non-TVR, see definitions below) both evaluated at long-term follow-up (at least 5 years).

Target Lesion Revascularization (TLR) was defined as ischemia-driven repeat PCI or surgical revascularization for intra-stent significant restenosis (≥50% by quantitative analysis) or for a significant stenosis at the proximal or dis-

Table 2. Procedural characteristics of patients with Rheumatoid Arthritis with coronary artery disease (RA-CAD+) stratified into 3 sub-groups of therapeutic management: percutaneous/surgical coronary revascularization (RA-PCI/RA-CABG) and medical therapy (MT)

Procedural Characteristics	RA-CAD+ (n=53)	RA-PCI (n=32)	RA-CABG (n=10)	RA-MT (n=11)	*P* value
Stable angina; n (%)	17 (32)	9 (28)	2 (20)	6 (54.5)	0.178
ACS					
NSTEMI; n (%)	6 (11)	5 (16)	0 (0)	1 (9)	0.382
STEMI; n (%)	16 (30)	12 (37.5)	2 (20)	2 (18)	0.357
Unstable angina; n (%)	5 (9.5)	5 (16)	0 (0)	0 (0)	0.163
Three-vessel disease; n (%)	14 (26.5)	3 (9)	10 (100)	1 (9)	<0.001
LAD; n (%)-D1; n (%)	19 (36)-5 (9.5)	11 (34)-2(6)	5 (100)-2 (40)	3 (27)-1 (9)	0.53-0.43
CX; n (%)-OM; n (%)	8 (15)-8 (15)	6 (19)-5 (16)	2 (40)-1 (20)	0 (0)-2 (18)	0.29-0.86
RCA; n (%)-IVP; n (%)	19 (36)-5 (9.5)	10 (31)-0 (0)	2 (40)-2 (40)	7 (64)-3 (27)	0.079-0.012
Three-vessel treatment; n (%)	-	0 (0)	4 (80)	-	<0.001
Complete revascularization; n (%)	-	18 (56)	4 (80)	-	0.091
Number of stent/patients; mean ± SD	-	1.09±0.47	-	-	-
Mean stent length, mm; mean ± SD	-	18.81±5.66	-	-	-
Mean stent diameter, mm; mean ± SD	-	3.21±0.38	-	-	-
Mean stent pressure, atm; mean ± SD	-	14.08±4.63	-	-	-
BMS; n (%)	-	18 (56)	-	-	-
DES; n (%)	-	14 (44)	-	-	-
Stent post-dilatation; n (%)	-	5 (16)	-	-	-
Angiographic success; n (%)	-	32 (100)	-	-	-

Data are presented as absolute numbers and percentages, for categorical variables, or mean value ± SD, for continuous variables. Percutaneous coronary intervention (PCI), Coronary artery bypass grafting (CABG), Medical therapy (MT), Left ventricular ejection fraction (LVEF), Body Mass Index (BMI), Non-ST elevated Myocardial Infarction (NSTEMI), ST elevated Myocardial Infarction (STEMI), Bare metal stent (BMS), Drug Eluting Stent (DES), Acute coronary syndrome (ACS), Left Anterior Descending artery (LAD), 1st diagonal (D1), Circumflex artery (CX), Obtuse Marginal (OM), Right Coronary artery (RCA), InterVentricular Posterior artery (IVP).

tal edge of the stent (5 mm either side of the stent). Target vessel coronary revascularization (TVR) was defined as ischemia-driven revascularization due to a restenosis in the target lesion or lesion elsewhere in the target vessel or its branches.

Single-vessel disease was defined as involvement of a major epicardial vessel with ≥70% stenosis or ≥50% stenosis of the left main. Multi-vessel disease was classified as ≥2 major epicardial vessels [9]. Procedural angiographic success after PCI was defined as the presence of residual coronary stenosis of ≤30% and final TIMI flow 3.

Coronary angiography was performed in case of a positive stress test (stress test, echo-stress, stress scintigraphy) or history of effort angina. Acute coronary syndrome (ACS) was defined as unstable angina, non-ST elevation myocardial infarction, or ST-elevation myocardial infarction according to the ESC guidelines [10, 11].

The medical anti-ischemic therapy (MT) regime was left to the discretion of the specialist and included antiplatelet agents, a statin, β-blocker, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker, and other anti-anginals (nitrates, sodium channel blockers) according to guidelines [12]. All clinical major events (death, cardiac death, stent thrombosis, myocardial infarction) were defined according to the Academic Research Consortium, ARC definition [13, 14].

Statistical analysis

Continuous and categorical variables are reported as mean ± standard deviation (SD), and as frequencies or percentages, respectively. Comparisons between groups were per-

formed using one-way ANOVA for continuous variables and using chi-square for categorical data.

Event-free survival curves, for MACCE and repeat revascularization, assessed at long term follow-up (at least 5-year) were evaluated according to the unadjusted Kaplan-Meier method and survival among groups were compared using the log-rank test (Cox-Mantel test). Two-sides *p*-values <0.05 were considered statistically significant.

The odds logistic regression analysis was used to test the independent relationship between clinical variables and primary and secondary end-points. To avoid multicollinearity, a "low-noise model" was used in which each predictor variable correlated minimally with the other. The selection of the variables included in the multivariable model was performed with backward elimination (Wald statistic, confirmed using forward and stepwise selection) based on the covariates listed in **Tables 1**, **2**. Only covariates that were significantly associated with primary and secondary end-points after univariate analysis (P<0.05 for model inclusion and P>0.10 for exclusion) were included. Results are reported as adjusted odds ratios (ORs) with 95% Confidence Intervals (CI).

Statistical analyses were performed using SPSS 16.0.2 (SPSS Inc., Chicago, IL, USA) and GraphPad Prism software (version 4; GraphPad, Inc, San Diego, CA).

Results

Clinical characteristics of overall study population (RA patients)

Out of 1003 patients with RA, a total of 936 patients were included in the study. Sixty-seven patients (7%) had incomplete baseline clinical information and were excluded (**Figure 1**).

The presence of clinically significant CAD was found in 53 patients (5.6%; defined RA-CAD+). The remaining 883 patients (94.4%) did not present significant CAD (RA-CAD-). Among RA-CAD+ patients, 11 patients (21%) were treated conservatively with MT (RA-MT group); 10 patients (19%) underwent coronary artery bypass grafting (RA-CABG group) and 32 patients (60%) underwent PCI (RA-PCI group), (**Figure 1**).

Clinical profile and procedural characteristics

Clinical characteristics are reported in **Table 1**. In particular, patients in RA-PCI group were significantly younger than those in the RA-CABG and RA-MT groups (mean age 64±9.7 vs 77±7 vs 75.9±9.8 years old, respectively; P<0.0001). In addition, patients in RA-PCI and RA-CABG groups were significantly more likely to be male compared with the RA-MT group (66% vs 60% vs 9% respectively; P=0.004). No other significant differences in clinical risk profile were present among study subgroups. Between groups, no significant differences were observed in terms of DAS28 score assessed at the time of the last rheumatologic ambulatory visit and before the coronary study.

In regard to medical therapy, most of the patients were on Disease-Modifying Anti-Rheumatic Drugs (DMARDs, 88.5% of study population) with the majority of them on Methotrexate (62%) and on steroid therapy (60%). Notably, no significant differences were recorded in rheumatologic or cardiologic therapy among subgroups with the exception of additional anti-angina drugs that were significantly more used in RA-MT group (P=0.001).

Procedural characteristics are reported in **Table 2**. The most common clinical presentation was acute coronary syndrome (68%). In addition, RA-CABG patients had a greater atherosclerotic burden compared with those in RA-PCI group (three-vessel disease in 100% of RA-CABG group versus 9% of RA-PCI group, P<0.0001). In RA-PCI patients, a mean of 1.09±0.47 stents (56% bare metal stents and 44% drug eluting stents) were implanted. Procedural angiographic success was achieved in all patients. No in-hospital adverse events were reported for patients who underwent PCI and only one (10%) perioperative myocardial infarction was recorded in the RA-CABG group.

Long-term clinical outcome

The clinical outcome of RA-CAD+ patients stratified into 3 subgroups is reported in **Table 3** and **Figure 2**. No difference in the mean follow-up time was observed between groups (9±5 vs 11±8.5 vs 10±6.1 years, RA-PCI vs RA-CABG vs RA-MT respectively; P=0.636). No statistically significant differences in the primary endpoint

Table 3. Clinical outcome of patients with rheumatoid arthritis (RA) and concomitant coronary artery disease (CAD) stratified for different CAD treatment (long-rank Mantel-Cox analysis)

Long-term clinical outcome	RA-CAD+ (n=53)	RA-PCI (n=32)	RA-CABG (n=10)	RA-MT (n=11)	*P* value
Years follow-up, mean ± SD	9±7	9±5	11±8.5	10±6.1	0.636
MACCE (primary endpoint)	26 (49)	18 (56)	5 (50)	3 (27)	0.184
All death	4 (7.5)	2 (6)	1 (10)	1 (9)	0.904
Cardiac death	4 (7.5)	2 (6)	1 (10)	1 (9)	0.904
ACS	9 (17)	8 (25)	0 (0)	1 (9)	0.136
NSTEMI	3 (5.5)	2 (6)	0 (0)	1 (9)	0.649
STEMI	3 (5.5)	3 (9)	0 (0)	0 (0)	0.352
Unstable angina	3 (5.5)	3 (9)	0 (0)	0 (0)	0.352
CABG	1 (2)	1 (3)	0 (0)	0 (0)	0.715
Stroke	4 (7.5)	0 (0)	3 (30)	1 (9)	0.007
TVR (per-patient)	-	12 (37.5)	0 (0)	-	0.022
TLR (per-patient)	-	9 (28)	0 (0)	-	0.058
Non TVR (per-patient)	-	10 (31)	1 (10)	-	0.182
Repeat revascularization (secondary endpoint)	17 (32)	15 (47)	1 (10)	1 (9)	0.017
Definite ST	-	2 (6)	-	-	-
Probable ST	-	0 (0)	-	-	-
Possible ST	-	1 (3)	-	-	-

Percutaneous coronary intervention (PCI), Coronary artery bypass grafting (CABG), Medical therapy (MT), major adverse cardiovascular and cerebrovascular events (MACCE), Acute coronary syndrome (ACS), Non-ST elevated Myocardial Infarction (NSTEMI), ST elevated Myocardial Infarction (STEMI), Target Vessel Revascularization (TVR), Target Lesion Revascularization (TLR), Stent Thrombosis (ST).

(MACCE) were found, even if there was a trend for higher MACCE rate at long-term outcome in RA-PCI and RA-CABG groups compared with RA-MT group (56% vs 50% vs 27%, respectively, P=0.184). Furthermore, a significantly higher rate of repeat revascularization (secondary endpoint) was observed in the RA-PCI group compared to RA-CABG and RA-MT groups (47% vs 10% vs 9%, respectively, P=0.017). In addition, a significantly higher rate of strokes was observed in RA-CABG group compared to RA-PCI and RA-MT groups (30% vs 0% vs 9%, respectively, P=0.007).

Furthermore, in the RA-PCI group, we observed 2 cases of cardiac death (6%, one occurred at 86 months and one at 39 months after index PCI, both due to ACS), and 12 cases of TVR (37.5%) and 9 cases of non-TVR (28% of patients). Three cases of definite stent thrombosis were reported (9%, at 37, 63 and 51 months after index procedure; one patient on double antiplatelet therapy and two patients on single antiplatelet therapy). In the RA-CABG group, we observed 1 cardiac death (10%, 109 months after surgery), 3 strokes (30%, at 3, 9 and 68 months after surgery) and 1 coronary revascularization by PCI (162 months after surgery). In the RA-MT group, we recorded 1 case of cardiac death (9%, 156 months after starting MT), 1 case of stroke (9%, 110 months after starting MT) and 1 case of NSTEMI (9%, 132 months after starting MT).

Interestingly, after multivariable analysis we found that the clinical presentation as STEMI at the index event was an independent risk factor for both primary and secondary endpoints at 15 years follow-up (MACCE: Odds Ratio OR 4.24, 95% Confidence Interval CI 1.09-16.52, P=0.038; repeat revascularization: OR 6.78, 95% CI 1.7-27, P=0.007). Chronic steroid therapy was also an independent protective factor for MACCE (Odds Ratio 0.24; 95% Confidence Interval 0.67-0.84, P=0.026).

Discussion

This study provides new data about long-term clinical outcomes of rheumatoid-arthritis patients with concomitant coronary artery dis-

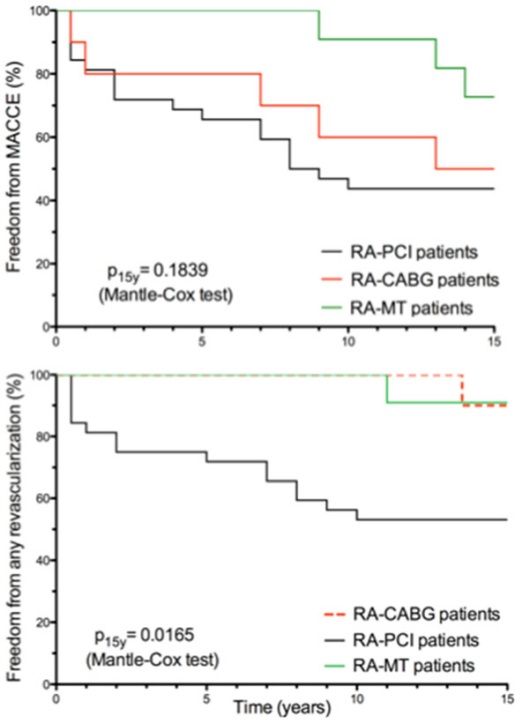

Figure 2. Kaplan-Meier estimates of freedom from MACCE (left panel) and revascularization (right panel) among RA patients after PCI (black), CABG (red) or managed with MT (green). RA, rheumatoid arthritis; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; MT, medical therapy; MACCE, major adverse cardiac events.

ease, stratified into three subgroups of therapeutic management: percutaneous, surgical coronary revascularization and medical therapy.

Gaps in evidence

There are only a few published reports exploring the clinical outcome of RA patients after coronary revascularization. On one hand, some retrospective studies [15, 16] have reported no differences or better outcomes in RA patients after coronary revascularization compared to non-RA patients. On the other hand, a recent large cohort study [17] reported that the risks of overall mortality and ischemic events after PCI were substantially higher in RA patients compared to controls. One of the major limitations of the latter study is that PCI was performed without stent implantation in almost half of the cases, leading to an uncommonly high rate of ischemic events and repeat revascularization both in the control (56% and 36%, respectively) and RA groups (61% and 32%, respectively). In addition, the same research group reported a large cohort study [18] evaluating the clinical outcomes of RA patients after CABG and reported a 30% of revascularization rate and about 60% mortality after 11-years follow-up. Furthermore, previous studies have reported a low intra-hospital cardiovascular event rate after coronary revascularization [19], which was consistent with our results. Summing it up, we do not have consistent and sufficient clinical evidence supporting a revascularization strategy (PCI or CABG) versus a conservative therapy (MT) in this high-risk subset of patients.

Study clinical outcomes: comparing management strategies

This is the first study evaluating the long-term clinical outcomes of a real-world tertiary-center study population of RA patients with concomitant CAD comparing 3 different management strategies. In our cohort no significant differences in primary clinical endpoint (MACCE) were found among the three different management strategies, even if there was a trend for higher rate of MACCE in patients who underwent coronary revascularization (56% in PCI-RA, 50% in CABG-RA) in comparison with patients treated conservatively (27% in RA-MT). Interestingly, in patients who underwent percutaneous coronary revascularization (RA-PCI) we found a significantly higher rate of secondary endpoint (any revascularization) during long-term follow-up when compared to other treatment strategies (**Figure 2**). A more detailed look at the data reveals that the high rate of MACCE (56%) in PCI patients was mainly driven by TVR (37.5%) whereas the rate of MACCE (50%) in CABG patients was chiefly driven by stroke (30%).

Poor clinical outcomes depicting a high-risk population

Despite the many limitations discussed below, the rate of cardiovascular events at follow-up in the revascularized patients was beyond what is expected after PCI and CABG in general population. Indeed, real-world PCI/CABG registries [20-24] reported the following results in a general population: 7% MACCE and 4% TVR in Nobori-2 population after PCI; 7% MACCE and

6% TVR in Resolute study after PCI; 40% MACCE and 7% any revascularization in the Kurlansky et al. study after PCI; 28% MACCE and 4% any revascularization in the Kurlansky et al. study after CABG.

Our data depict a very-high-risk population in need of better clinical awareness and procedural management. Once PCI is chosen as the appropriate revascularization option, we should be aware that these patients are probably at risk for repeat coronary revascularizations. However, the adoption of interventional strategies including more meticulous and aggressive lesion preparation (balloon non-compliant predilatation, debulking techniques), the use of newer generation drug-eluting stents and intravascular imaging may potentially help preventing adverse ischemic events. Prospective studies focusing on these issues are needed. Furthermore, there is an emerging need to investigate possible risk and protective factors for worse clinical outcomes in these patients. In our small study cohort we found on multivariable analysis that STEMI was an independent risk factor for both MACCE and coronary revascularization during follow-up. Notably, none of the traditional risk factors for CAD proved to be an independent predictor for study endpoints. The interpretation of these results is uncertain because of the small sample size and the lack of etiologic markers supporting any hypothesis. However, these results could be hypothesis generating for basic research studies focusing on unstable CAD in RA patients.

Limitations

The study results must be interpreted in the light of the major limitations related to the low sample size in each group and therefore the direct comparison between groups was certainly underpowered. In order to derive more robust conclusions, a multi-center study with a greater number of patients is needed. The low use of statin among study patients, mainly due to the fact that many CAD diagnosis were performed before international guidelines started recommending them, may have played a role in the adverse clinical outcome of these patients. The present study includes other limitations, related to the "real-world" retrospective design. Firstly, it was non-randomized. Secondly, the retrospective nature and the relatively small study population of CAD patients cannot exclude the possibility of "clinical selection" bias between the 3 subgroups, which could favor the clinical outcome of MT patients.

Conclusion

Our study provides new data about the long-term clinical outcomes of RA patients with clinically significant CAD. An overall high rate of ischemic events was observed, especially in patients who underwent coronary revascularization with either PCI or CABG. These results are hypothesis generating for further prospective studies involving larger populations of RA-CAD+ patients and call for better clinical awareness and procedural management of these high-risk patients.

Disclosure of conflict of interest

None.

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