Radial access versus femoral access in myocardial infarction – a single-center experience

Radialni pristop v primerjavi s femoralnim pristopom pri bolnikih z miokardnim infarktom – naše izkušnje

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Abstract

Background: Data on the relationship between radial access (RA) and outcome in patients with myocardial infarction (MI) undergoing percutaneous coronary intervention (PCI) are inconclusive. The aim of our study was to assess whether RA *per se* is associated with 30-day mortality in patients with MI undergoing percutaneous coronary intervention in our centre or whether the possible benefit of RA is the result of reduced bleeding and/ other confounding factors.

Methods: We retrospectively studied 3501 consecutive patients with MI who underwent PCI between January 2012 and December 2016. The 30-day mortality rates in the RA and femoral access (FA) groups were observed. Data were analysed using descriptive statistics.

Results: RA patients had a significantly lower 30-day unadjusted mortality [53 (3.8 %) patients died in the RA group compared to 207 (9.8 %) patients in the FA group; p < 0.0001]. After adjusting for confounders, the difference was no longer significant (adjusted OR: 0.84; 95 % CI: 0.58 to 1.22). Cardiogenic shock, age over 70 years, hypertension, hyperlipidaemia, anaemia on admission, renal dysfunction on admission, ST-elevation MI, bleeding, and the contrast volume/ GFR ratio predicted 30-day mortality. However, RA was not found to predict 30-day mortality.

Conclusion: RA provides a better 30-day outcome in patients with MI (ST-elevation MI and non--ST-elevation MI) undergoing PCI. However, our result suggests that the better outcome with RA in daily practice in our centre is probably causatively linked to a reduced bleeding rate rather than to RA *per se*.

Izvleček

Izhodišče: Radialni pristop postaja vodilni pristop za perkutano koronarno intervencijo (PCI). Podatki o tem, ali že sam pristop zagotavlja boljše rezultate, ali pa so ti posledica manjšega števila krvavitev, zapletov in različno bolnih bolnikov, so nepopolni in si delno nasprotujejo. Namen naše raziskave je bil ugotoviti, ali je radialni pristop sam po sebi povezan s 30-dnevno umrljivostjo pri bolnikih z miokardnim infarktom, ki so imeli opravljeno PCI v našem centru, ali pa je morebitna dobrobit posledica manjšega števila krvavitev in drugih dejavnikov.

Metode: Retrospektivno smo obdelali podatke zaporednih 3.501 bolnika z miokardnim infarktom, ki so imeli PCI v našem centru med januarjem 2012 in decembrom 2016. Primerjali smo 30-dnevno umrljivost pri bolnikih z radialnim in bolnikih s femoralnim pristopom. Podatke smo statistično ustrezno obdelali.

Rezultati: Bolniki z radialnim pristopom so imeli manjšo 30-dnevno umrljivost kot bolniki s femoralnim pristopom. Umrlo je 53 (3,8 %) bolnikov z radialnim pristopom in 207 (9,8 %) bolnikov s femoralnim pristopom; p < 0.0001. Po upoštevanju ostalih dejavnikov v multifaktorski anali-

zi razlika v umrljivosti ni bila več statistično pomembna (razmerje obetov (OR): 0.84; 95 % CI: 0.58 to 1.22). Dejavniki, ki so napovedovali umrljivost, so bili kardiogeni šok, starost nad 70 let, hipertenzija, anemija in ledvična okvara ob sprejemu, miokardni infarkt z dvigom veznice ST, krvavitev, razmerje med volumnom kontrasta in glomerulno filtracijo, ne pa tudi radialni pristop.

Zaključek: Radialni pristop v naši raziskavi ni neodvisno napovedoval 30-dnevne umrljivosti pri bolnikih z miokardnim infarktom, ki so imeli opravljeno PCI. Naši rezultati nakazujejo, da je bil boljši izid zdravljenja bolnikov z radialnim pristopom povezan z drugimi dejavniki, predvsem s krvavitvijo in hemodinamskim iztirjenjem.

1 Introduction

Radial access (RA) has been increasingly used in interventional cardiology, and it has become the dominant access site for percutaneous coronary intervention (PCI) (1,2). RA is more advantageous than femoral access (FA) in terms of patient comfort and early ambulation. It has also been proven to decrease vascular access complications and bleeding, and to improve the prognosis compared to femoral access (FA) in patients with myocardial infarction (MI) undergoing percutaneous coronary intervention (PCI) (1-5). The data on the association between RA *per se* and a better outcome, and whether the better result is due to a lower complication rate, are still inconsistent and inconclusive (1,3,4,6-9).

Generalising the findings of randomised trials to clinical practice also has limited application (10). These trials tend to include younger patients, fewer females, and patients with less anaemia and/or kidney disease. Nowadays, the superiority of RA over FA may be attenuated due to the smaller arterial sheaths and targeted anticoagulant agents that reduce the risk of bleeding (3).

The current non-ST-elevation MI and ST-elevation MI guidelines of the European Society of Cardiology give an IA recommendation for radial PCI if performed by an experienced operator (11,12) There are still large regional and national variations in the use of RA in patients with MI.

RA was introduced to our centre in 2010 and has been increasingly used in patients with MI since 2012. In 2016, RA became the predominant access site for PCI in patients with MI. The aim of our study was to assess whether RA itself is associated with 30-day mortality in patients with ST-elevation MI and non-ST--elevation MI undergoing PCI in our centre, or whether the possible benefit of RA is the result of reduced bleeding and other confounding factors.

2 Methods

The retrospective, single-center observational study was performed at the University Medical Centre Maribor, a tertiary referral hospital with a 24/7 primary PCI service. The study group comprised 3765 consecutive MI (ST-elevation MI and non-ST-elevation MI) patients who had undergone PCI between January 2012 and December 2016.
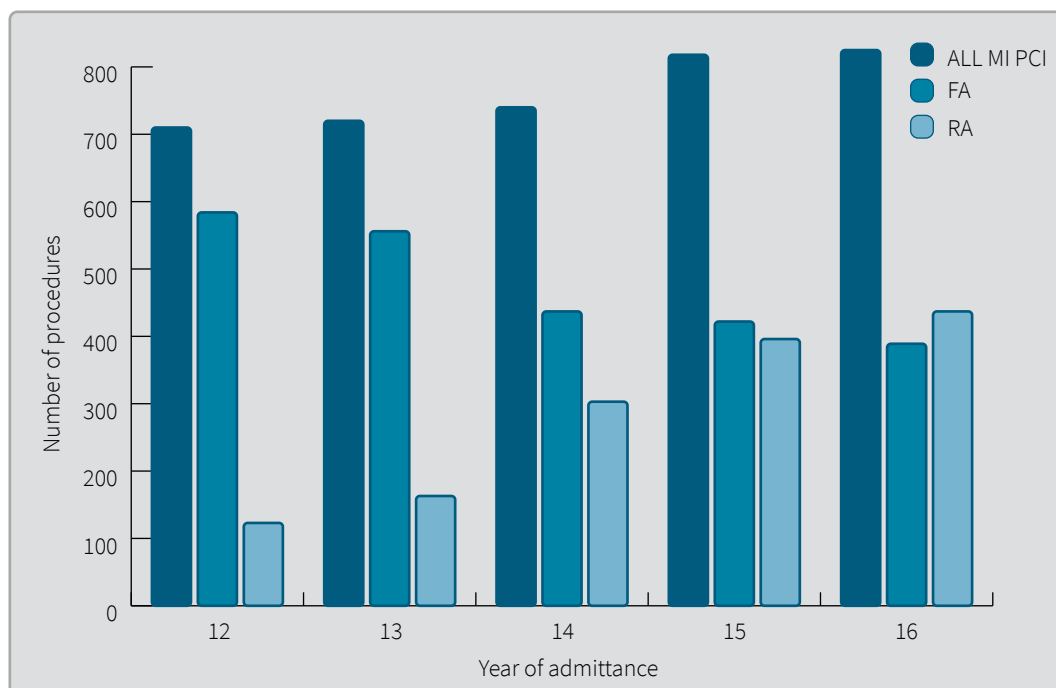
Figure 1: Number of patients with myocardial infarction and radial or femoral access stratified by year of admission.

RA PCI in non-ST-elevation MI patients has been performed at our Centre since 2011. In the first year, the numbers were so small (23 patients with non-ST--elevation MI and 3 patients with ST-elevation MI) that we did not include patients from 2011 in the analysis.

The groups with RA patients and FA patients were compared. This was an all-comers study. Thrombolysis was not used. All the medical records were gathered from the hospital information system to complete the data collection.

The definition of MI was based on the relevant guidelines (11,12)

Cardiogenic shock (CS) was defined according to clinical and haemodynamic criteria, including hypotension (systolic blood pressure ≤ 90 mm Hg for ≥ 30 minutes or the need for supportive measures to maintain a systolic blood pressure of > 90 mmHg) and evidence of end-organ hypoperfusion. Anaemia was

defined as proposed by the World Health Organization: a serum haemoglobin level < 130 g/L for men and < 120 g/L for women (13)

The Bleeding Academic Research Consortium (BARC) bleeding criteria and BARC 3a bleeding (Hb drop of 30–50 g/L or any transfusion) were used (14). Renal dysfunction was defined as a glomerular filtration rate (GFR) less than 60 ml/kg/1.73 m^2 on admission. GFR was calculated using the 4-variable Modification of Diet in Renal Disease formula (15). Thrombolysis in Myocardial Infarction (TIMI) flow grades were used for assessment of coronary flow (16).

Patients were treated according to the guidelines for the management of MI (11,12). The angioplasty strategy, access site, and concomitant medication were left to the discretion of the operator Data on all essential patient and proced-

ural characteristics were 95.2 % complete and ascertainment of bleeding and mortality were 99.1 % and 100 % complete, respectively. The study was approved by the local ethics committee.

Research was approved by Ethical Committee for Medical Research at University Medical Centre Maribor, on 3. March 2019 (ref.: UKC-MB-KME-24/19).

2.1 Outcome

The end point was the 30-day mortality in the RA and FA groups of MI patients (ST-elevation MI and non-ST--elevation MI). The post hoc secondary outcome was BARC3a bleeding.

2.2 Statistical methods

2.2.1 Power analysis

Following Hsieh estimates (17) a total of 3501 patients were calculated to have a > 95 % power to detect a significant association for logistic regression (using alpha of 0.05, 30-day mortality rate of 8 %, medium odds ratio of about 1.5 to 1 (18), and a variance inflation factor of 1.35). The variance inflation factor, which depends on the squared multiple correlation coefficient (R^2) relating a specific predictor of interest to the remaining predictors, was calculated according to the model of Hsieh et al. (19). Our study design did not involve one specific predictor of interest, hence we calculated R^2 for each predictor in the model and used the maximum value obtained. For continuous predictors selected as dependent variables, we applied linear regression to calculate standard R^2. For categorical predictors selected as dependent variables, we applied logistic regression and calculated Nagelkerke R^2.

2.2.2 Data analysis

Distributions of continuous variables in the two groups were compared with either the two-sample *t*-test or the Mann-Whitney test according to whether the data followed the normal distribution. Distributions of categorical variables were compared with the chi--square test. All p-values were two-sided; p-values less than 0.05 were considered statistically significant.

Binary logistic regression modeling was used to calculate the adjusted odds of 30-day mortality. The models were adjusted for age, gender, diabetes, hyperlipidaemia, hypertension, renal dysfunction on admission, anaemia on admission, ST-elevation MI, cardiogenic shock, bleeding, the contrast volume/GFR ratio, and RA. Data were analysed using the SPSS 22.0 software for Windows (IBM Corp., Armonk, NY).

3 Results

3.1 Descriptive data for patients before PCI

Of the 3765 MI patients, PCI with RA was planned in 1633 (43.4 %). A graded increase in RA was observed, with it becoming the predominant access site in 2016 (Figure 1).

The majority of the 264 patients undergoing PCI who needed crossover were in the group with intended RA [248 (93.9 %) patients], while only 16 (6.1 %) patients needed crossover from FA to RA. After performing the intention-to-treat analysis in all patients, regardless of whether they crossed over to another access site, we excluded patients who required crossover from RA to FA or vice versa [264 (7.0 %)], leaving 3501 (93.0 %) patients for further analysis.

The RA patient group had less diabetes and suffered less frequently from renal dysfunction and anaemia on admission. On the contrary, they presented more often with hypertension and hyperlipidaemia.

They were less likely to suffer ST-elevation MI, and less likely to present with cardiogenic shock. Fewer angioplasties of the left main coronary artery and the left anterior descending artery were performed in this group, but more were performed in the circumflex artery. Multivessel PCI was found less often in the RA patients.

A larger volume of contrast and a higher contrast volume/GFR ratio were used in the RA group. Bivalirudin and adjunctive therapy with GP IIb/IIIa receptor inhibitors were also less often administered to patients with RA, and less bleeding after PCI occurred in this group.

There were substantial differences in the basic clinical, angiographic, and therapeutic characteristics of patients in the two groups, as shown in Table 1 and Table 2.

3.2 30-day mortality

3.2.1 Intention-to-treat analysis

After 30 days, less patients with RA died [56 (4.0 %) compared to 231 (9.8 %) patients with FA; $p < 0.0001$]. After adjustment for confounders, RA alone was not independently associated with 30-day mortality (adjusted OR: 0.99; 95 % CI: 0.63 to 1.30).

After exclusion of all patients who required crossover from RA to FA or vice versa, RA patients had a significantly lower 30-day unadjusted mortality [53(3.8 %) patients died in the RA group compared to 207(9.8 %) patients in the FA group; $p < 0.0001$]. The unadjusted RA-to-FA odds ratio for 30-day mortality was 0.38 (95 % confidence interval 0.27 to 0.50; $p < 0.0001$).

After adjustments for confounders, the difference was no longer significant (adjusted OR: 0.84; 95 % CI: 0.58 to 1.22). Cardiogenic shock, age over 70 years, hypertension, hyperlipidaemia, anaemia on admission, renal dysfunction on admission, ST-elevation MI, bleeding, and the contrast volume/GFR ratio predicted

Table 1: Basic clinical characteristics of patients

	Femoral access N = 2116	Radial access N = 1385	p
Age, years[†]	65 1 (12.1)	64.4 (11.8)	0.13
Male gender, N (%)*	1462 (69.1)	981 (70.8)	0.27
Diabetes, N (%)*	497 (23.5)	283 (20.4)	0.034
Hypertension, N (%)*	1138 (53.8)	816 (58.9)	0.003
Dyslipidaemia, N (%)*	819 (38.7)	588 (42.5)	0.029
Anaemia, N (%)*	656 (31.2)	275 (19.9)	<0.0001
Renal dysfunction, N (%)*	452 (21.6)	238 (17.2)	0.002
ST-elevation MI, N (%)*	1437 (67.9)	572 (41.3)	<0.0001
Cardiogenic shock, N (%)*	159 (7.5)	21 (1.5)	<0.0001

[†] Mean (standard deviation); comparison made using the t-test.; * Comparison made using the chi-square test. N = number.

30-day mortality, but RA *per se* did not (Table 3).

Subgroup analyses across different clinical syndromes also revealed that RA was not associated with 30-day mortality. RA was not associated with the outcome in either ST-elevation MI patients (572 RA patients compared to 1437 FA patients: OR 0.86; 95 % CI 0.56 to 1.31), or non-ST-elevation MI patients (813 RA patients compared to 679 FA patients: OR 0.88; 95 % CI 0.40 to 1.93).

3.3 Bleeding

Barc 3a bleeding (Hb drop of 30–50 g/L or any transfusion) occurred less often in the RA group [45 (3.3 %) patients in the RA group compared to 170 (8.0 %) patients in the FA group; p < 0.0001]. The unadjusted RA-to-FA odds ratio for bleeding was 0.38 (95 % confidence interval 0.27 to 0.53; p < 0.0001). Independent predictors of bleeding were RA (adjusted OR 0.53 (95 % CI 0.37 to 0.76; p < 0.0001), anaemia on admission (adjusted OR 1.81 (95 % CI 1.32 to 2.49; p < 0.0001), renal dysfunction (adjusted OR 2.41 (95 % CI 1.70 to 3.42; p < 0.0001), cardiogenic shock (adjusted OR 3.44 (95 % CI 2.49 to 5.26; p < 0.0001), and hyperlipidaemia (adjusted OR 1.89 (95 % CI 1.39 to 2.68; p < 0.0001).

Table 2: Procedural characteristics

	Femoral access N = 2116	Radial access N = 1385	p
P2Y12 receptor inhibitors, N (%)*	1919 (90.7)	1230 (88.8)	0.075
GP IIb/IIIa receptor inhibitors, N (%)*	719 (34.0)	254 (18.3)	<0.0001
Bivalirudin, N (%)*	346 (16.4)	149 (10.8)	<0.0001
PCI-left main coronary artery, N (%)*	108 (5.1)	22 (1.6)	<0.0001
PCI-left anterior descending artery, N (%)*	901 (42.6)	514 (37.1)	0.001
PCI-circumflex artery, N (%)*	429 (20.3)	334 (24.1)	0.007
PCI-right coronary artery, N (%)*	654 (30.9)	388 (28.0)	0.07
Multivessel PCI. N (%)*	354 (16.1)	195 (14.1)	0.037
TIMI flow 0/1 after PCI, N (%)*	138 (6.5)	85 (6.1)	0.67
Contrast volume, ml[†]	152.0 (113.0, 205.0)	171.0 (125.0, 230.0)	<0.0001
Contrast volume/GFR ratio[†]	1.90 (1.27, 2.91)	2.04 (1.44, 3.10)	<0.0001
Bleeding, N (%)*	170 (8.0)	45 (3.3)	<0.0001

* Comparison made using the chi-square test; [†] Median (25th, 75th percentile); comparison made using the Mann-Whitney test. GFR = glomerular filtration rate; N = number; PCI = percutaneous coronary intervention; TIMI flow = Thrombolysis In Myocardial Infarction grade flow.

4 Discussion

The intention of our work was to analyse the result of RA usage in our centre in patients with MI (ST-elevation MI and non-ST-elevation MI). We retrospectively analysed patients with MI who underwent PCI. We found, as had others before us, that patients with RA have a better outcome (1,2,4-9). Patients in the RA group were found to have a lower unadjusted 30-day mortality. However, after adjustment for potential confounders, RA *per se* was not identified as an independent predictive factor for 30-day mortality.

There may be several reasons why the significantly better 30-day unadjusted survival in patients with RA was not reflected in an association between RA and improved mortality.

A majority of ST-elevation MI patients with severer coronary artery disease (more angioplasties of the left main coronary artery and left anterior descending artery) were included in the FA group. These patients presented more often with cardiogenic shock, which all predict higher mortality (11,12).

Bleeding, which, according to the definition used, also includes transfusion, was more common in the FA group. Bleeding is associated with a poorer outcome after PCI (19). Substantial acute blood loss could impair the ability to recover after myocardial injury. A lower haemoglobin level decreases oxygen delivery to the tissues and myocardium (20,21). The compensatory response is a larger stroke volume and higher heart rate, which result in increased myocardial oxygen demand (22). This demand cannot be met in the setting of lower haemoglobin and ischaemia since the oxygen supply is already decreased (22).

Renal dysfunction on admission was more common in the FA group. Renal dysfunction is one of the factors predisposing to higher mortality in MI patients (11,12) Patients with renal dysfunction also suffered more bleeding (14.5 % vs. 4.2 %; p < 0.0001), as previously reported (11,12)

Table 3: Prognostic factors for 30-day mortality

	OR	95 % CI	p
Cardiogenic shock	14.55	9.74–21.74	<0.0001
ST-elevation MI	3.39	2.21–4.94	<0.0001
Age ≥ 70 yrs	2.21	1.55–3.14	<0.0001
Renal dysfunction on admission	1.96	1.36–2.84	<0.0001
Bleeding	1.93	1.24–3.01	0.004
Hypertension	1.90	1.36–2.56	<0.0001
Dyslipidemia	1.74	1.18–2.56	0.005
Anaemia on admission	1.52	1.08–2.13	0.016
Contrast volume / GFR	1.04	1.02–1.07	0.001

CI = confidence interval, GFR = glomerular filtration rate, OR = odds ratio.

Patients in the FA group were more anaemic on admission. Anaemia *per se* was found to be a risk factor for higher mortality in patients with MI (21-24) In the setting of myocardial infarction, anaemia worsens ischaemia by reducing oxygen delivery to the injured myocardium (22). Significantly, the inflammatory state due to MI may result in suppression of erythropoiesis and the intestinal absorption of iron (25). Adaptation to anaemia may lead to left ventricle dilatation and eccentric remodelling, which could be particularly deleterious in the post-infarction period (25). In addition, neurohumoral activation is expected to be greater and may persist after the acute phase of MI. This may be one of the mechanisms that lead to cardiac remodelling and heart failure (25). Furthermore, bleeding was seen more often in anaemic patients (11.5 % vs. 4.2 %; p < 0.0001), which is in line with previous observations (26).

All the above-mentioned facts elucidate the worse outcome in FA patients in our analysis.

A higher contrast volume/GFR ratio was found In the RA group. This ratio was associated with 30-day mortality. In fact, the CV/GFR ratio did not differ between FA and RA patients who died [2.73 (1.64, 4.39) in RA patients compared to 3.20 (1.76, 4.96) in FA patients; p = 0.43]. The contrast volumes used in RA were larger than in FA. This may suggest that operators were less familiar with RA than FA. However, the volume of contrast used in our patients was lower than in similar studies, which speaks in favour of the experience of our RA team (27,28). Nevertheless, Ando et al. previously found that a potential increase in contrast volume load (compared to FA) is unlikely to have any impact on the benefit of RA (29).

Results from previous studies "suggest that a reduction in all-cause deaths with radial access could be mediated by a reduction of bleeding events« (4) and that there is "a causative link between major bleeding and death« (30). Therefore, even landmark prospective trials and meta-analyses do not claim that the better patient outcome is causatively linked to the access site *per se*. Data from daily practice show that RA is associated with the outcome in patients with MI without cardiogenic shock (1).

Randomised trials do not include very sick patients, so comparisons with "real life" data must be made in light of these differences. These study populations tend to have younger patients, fewer females, and patients with less anaemia and/ or kidney disease than populations from clinical experience (10). Our population consisted of MI patients only (acute coronary syndrome in Matrix), more patients with ST-elevation MI and more women (4). Furthermore, more patients with cardiogenic shock were included (4)

Previous fibrinolysis was not used, while more IIb/IIIa receptor antagonists were used in our daily practice (4). Consequently, more bleeding occurred after PCI (4). Patients in our analysis were also more often anaemic on admission and anaemia was used in calculations, which was not the case in Matrix (27).

It could be expected that sicker patients, with a predominance of women, a higher prevalence of cardiogenic shock and more potent antiplatelet therapy would end up with more bleeding. Bleeding might, therefore, be even more important for the outcome in such patients. In our opinion, these differences could explain our result, which is in line with the previous finding.

Our result (with all its limitations) suggests that the benefit of RA in daily practice in our centre is most probably causatively linked to a reduced bleeding rate rather than to RA *per se*, which has also been found previously (4,30). Unfortunately, we do not have the data on other complications after PCI.

Why do operators still choose FA? In real life, operators obviously choose FA in sicker patients who present with haemodynamic impairment where the access site needs to provide a quick and reliable path for opening the coronary artery. In such patients, there is the potential for RA failure requiring conversion to FA (puncture failure or failure to advance in RA) (2). Even in prospective studies (which do not include the sickest patients), the conversion rate is 3.7 %-7.6 %, depending on the operators' experience (2,10). Crossover increases the procedure time, which might impact the outcome in high-risk patients. Significantly, RA does not provide access for potential mechanical haemodynamic support, which may become extremely important in cardiogenic shock (2).

Our data support the supposition that operators want to be able to operate quickly through bigger guiding catheters with more devices simultaneously in case of emergent situations in very sick patients. FA enables such a procedure but at the cost of more intra- and post-procedural bleeding.

Our finding has some potential clinical implications. Whenever possible, PCI in MI patients should be performed with RA in order to decrease bleeding and other complications to improve the outcome. Whether this is also true for most endangered patients with CS, patients with ongoing resuscitation, and patients who need mechanical circulatory support, is still to be determined in future research.

4.1 Limitations

This was an observational, retrospective, single-centre study. Our data encompassed all-cause mortality only. A selection bias was present because the access site was left to the discretion of the operators. The data on blood pressure on admission and evidence-based medical therapy (except for P2Y12 receptor antagonists) after PCI and data on complications of PCI were not available. There were no exclusion criteria regarding concomitant diseases or clinical presentation, hence this population represents a real-world experience of high-risk patients requiring PCI. In multivariate analysis, rather wide CIs were present, which lowers the strength of our analysis.

5 Conclusion

RA provides a better 30-day outcome in patients with MI (ST-elevation MI and non-ST- elevation MI) undergoing PCI. RA was associated with a reduced risk of bleeding, but it did not independently predict mortality. This result suggests that the better outcome with RA in daily practice in our centre is probably causatively linked to a reduced bleeding rate rather than to RA *per se*.

6 Funding

7 Conflict of interest

The authors declare that there is no conflict of interest.

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