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Pharmacological therapy for the prevention of cardiovascular events in patients with myocardial infarction with non-obstructed coronary arteries (MINOCA): Insights from a multicentre national registry

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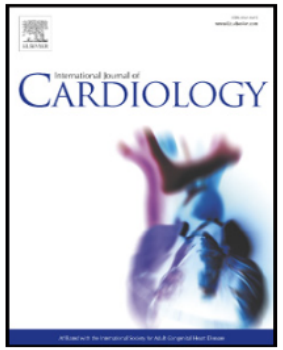

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ABSTRACT

Aims: To assess the effect of pharmacological therapy on long-term prognosis of patients with MINOCA.

Methods and results: In this retrospective multicentre cohort study involving 9 Hub Hospitals across Italy we enrolled consecutive patients 18 years and older with diagnosis of MINOCA discharged from 1st March 2012 to 31st March 2018. Data on baseline characteristics and pharmacological therapy at discharge (ACEI/ARB, angiotensin-converting enzyme inhibitors/angiotensin receptor antagonists; ASA, acetylsalicylic acid; beta-blockers; CCB, calcium-channel blockers; DAPT, dual anti-platelet therapy; statins), were collected systematically. The primary endpoint (PE) of the study was a composite of all cause death or acute myocardial infarction or acute coronary syndrome or heart failure leading to hospitalization or stroke.

A total of 621 patients were included (mean [SD] age 65.1 [13.9] years; 344 [55.4%] female), of whom 106 (17.1%) experienced PE, including 27 patients (4.3%) who died.

Multivariable analysis, after correction for all baseline differences, showed a significant association between pharmacological therapy at discharge and an increased risk of PE for aspirin (HR[95%CI] = 2.47[1.05–5.78], adjusted $p = 0.04$), whereas beta-blockers were associated with a significant benefit (HR[95%CI] = 0.49 [0.31–0.79], adjusted $p = 0.02$).

Conclusion: The use of beta-blockers was significantly associated to a less frequent occurrence of adverse outcomes at long-term follow-up among patients with MINOCA, whereas ASA displayed a potentially harmful impact on prognosis. The findings in the study may be relevant for the design of future studies which should take into account possible heterogeneity among MINOCA patients.

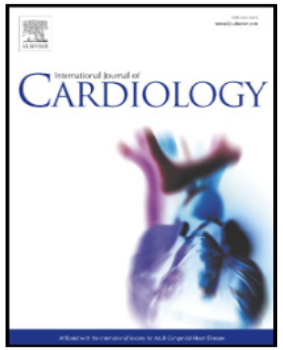

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Table 1.

	Total, $n = 621$	PE, $n = 106$	No PE, $n = 515$	P value
Demographics				
Age (±SD)	65.1 ± 13.9	67.3 ± 14.5	64.6 ± 13.8	0.073
Age ≥ 75 years	28.2	22.3	15	0.05
Female (%)	55.4	47.2	57.1	0.068
Medical history, %				
Hypertension	61.4	72.5	59	0.013
Diabetes mellitus	16.1	24.5	14.3	0.017
Hyperlipidaemia	45.1	39.4	46.3	0.224
Smoking	30.7	32.5	30.4	0.570
CAD family history	28.5	20.8	30.1	0.001
AF history	12.5	19.8	11.1	0.036
COPD	4.5	9.3	3.7	0.062
Cerebrovascular disease	5.1	9.3	4.4	0.084
Prior AMI (%)	5.6	6.8	5.4	0.590
ECG at admission, %				
ST-elevation	17.7	34.9	14.2	<0.001
LVEF < 50% (admission), %	25.1	33.0	23.5	0.049
CMR-confirmed MINOCA, %	21.6	26.4	20.6	0.195
Acute complications, %	4.2	1.1	3.1	0.393
Angiographic characteristics, %				0.02
NCA	56.9	43.9	59.3	
1–2 vessels MCAD	35.6	41.8	34.4	
3 vessels/LMS MCAD	7.5	14.3	6.2	
Blood testings				
Creatinine (mg/dl)	1.09 ± 0.5	1.0 ± 0.0	1.1 ± 0.6	0.679
Haemoglobin (g/dl)	13.2 ± 1.6	12.9 ± 1.6	13.6 ± 1.6	0.526

Baseline characteristics and univariate analysis for the primary endpoint (PE).
AF, atrial fibrillation; AMI, acute myocardial infarction; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; LMS, left main stem; LVEF, left ventricular ejection fraction; MCAD, mild coronary artery disease; NCA, normal coronary arteries; PE, primary end-point.

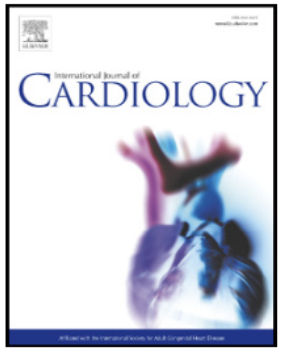

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Table 2.

	Total, n = 621	PE, n = 106	No PE, n = 515	P value
ASA (%)	87.9	93.4	86.8	0.070
DAPT (%)	58.8	60.0	58.5	0.816
P2Y12-I (%)	60.3	57.4	60.9	0.564
Beta-blockers (%)	69.4	60.4	71.3	0.033
ACEI (%)	57.1	58.5	56.8	0.829
ARB (%)	14.5	19.5	13.7	0.114
Statins (%)	81.0	80.2	81.2	0.787
CCB (%)	22.7	26.8	21.9	0.320

Pharmacological therapy and univariate analysis for the primary endpoint (PE).
ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin-receptor blockers; ASA, acetylsalicylic acid; CCB, calcium-channel blockers; DAPT, dual anti-platelet therapy; PE, primary end-point; P2Y12-I, P2Y12-inhibitors.

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Table 3.

	Primary endpoint		Unadjusted HR (95% CI)	Unadjusted P value	Adjusted HR (95% CI)	Adjusted P value
	PE (n = 106)	No PE (n = 515)				
ASA (n = 546)	99 (93.4)	447 (86.8)	2.09 (0.97–4.49)	0.060	2.47 (1.05–5.78)	0.04
No ASA (n = 75)	7 (9.3)	68 (13.4)	0.65 (0.30–1.14)			
DAPT (n = 325)	54 (50.9)	271 (52.6)	1.04 [0.68–1.59]	0.86	2.25 [0.58–8.79]	0.24
No DAPT (n = 296)	52 (49.1)	244 (47.4)	0.95 (0.60–1.51)			
P2Y12-I (n = 339)	54 (50.9)	285 (55.3)	0.84 [0.56–1.27]	0.41	0.45 [0.22–1.68]	0.24
No P2Y12-I (n = 282)	52 (49.1)	230 (44.7)	1.17 (0.74–1.86)			
B-blockers (n = 402)	61 (57.6)	341 (66.2)	0.62 (0.41–0.92)	0.02	0.49 (0.31–0.79)	0.02
No B-blockers (n = 219)	45 (42.4)	174 (33.8)	1.24 (1.02–2.37)			
ACEI/ARB (n = 430)	78 (73.6)	352 (68.4)	1.29 [0.83–1.99]	0.26	0.70 [0.40–2.21]	0.21
No ACEI/ARB (n = 191)	28 (26.4)	163 (31.6)	0.79 (0.64–1.07)			
Statins (n = 503)	85 (80.2)	418 (81.2)	1.05 [0.65–1.69]	0.86	1.67 [0.91–3.05]	0.10
No Statins (n = 118)	21 (19.8)	97 (18.8)	0.83 (0.49–1.39)			
CCB (n = 123)	22 (20.8)	101 (19.6)	1.14 [0.69–1.88]	0.61	1.41 [0.77–2.5]	0.27
No CCB (n = 498)	84 (79.2)	414 (80.4)	0.67 (0.45–0.97)			

Multivariate Cox model analysis for the primary endpoint (PE) according to commonly indicated pharmacological agents.
ACEI/ARB, angiotensin-converting enzyme inhibitors/angiotensin receptor antagonists; ASA, acetylsalicylic acid; CCB, calcium-channel blockers; DAPT, dual anti-platelet therapy; PE, primary endpoint; P2Y12-I, P2Y12-inhibitors.

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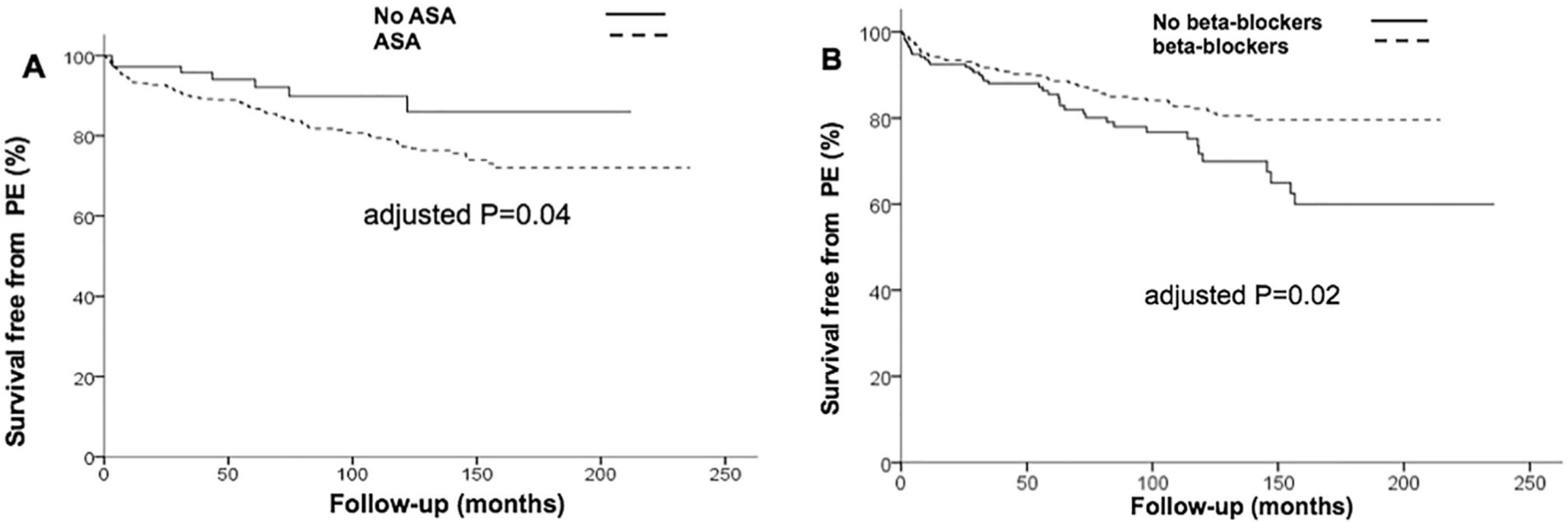
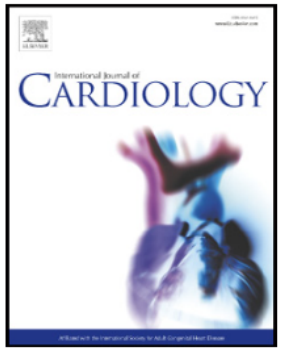


Fig. 1. 1A, Kaplan–Meier curves for the combined primary endpoint (PE) according to the prescription of acetylsalicylic acid (ASA) at discharge versus no prescription. 1B, Kaplan–Meier curves for the combined primary endpoint (PE) according to the prescription of beta-blockers at discharge versus no prescription.



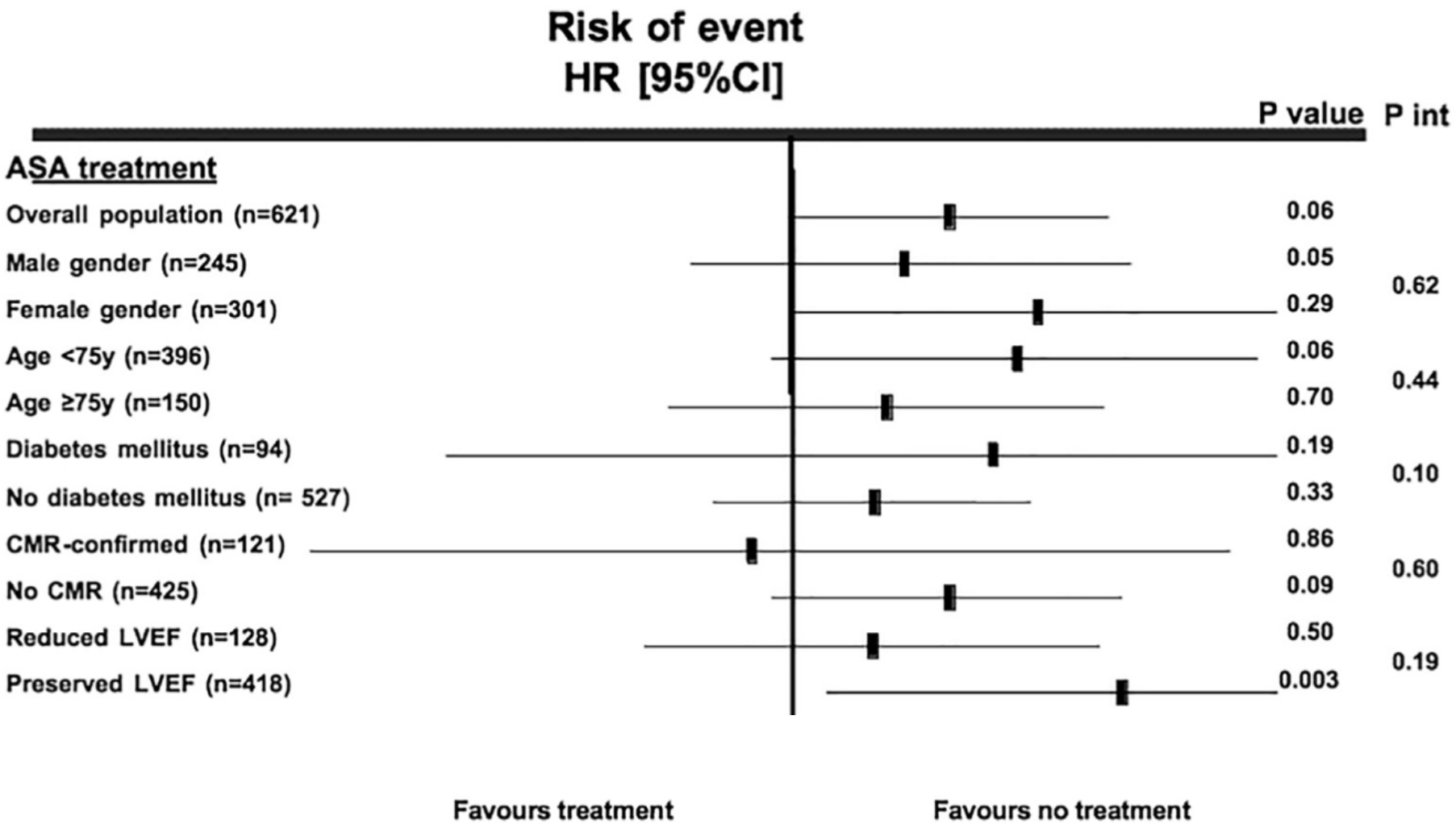
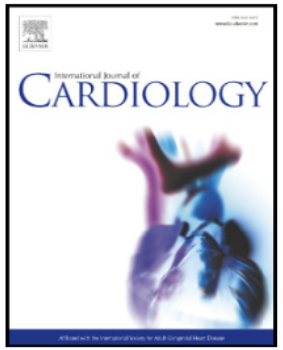


Fig. 2. Forest plot analysis for the risk of the combined primary endpoint (PE) in major higher risk subsets of patients according to the use of acetylsalicylic acid (ASA) and beta-blockers.



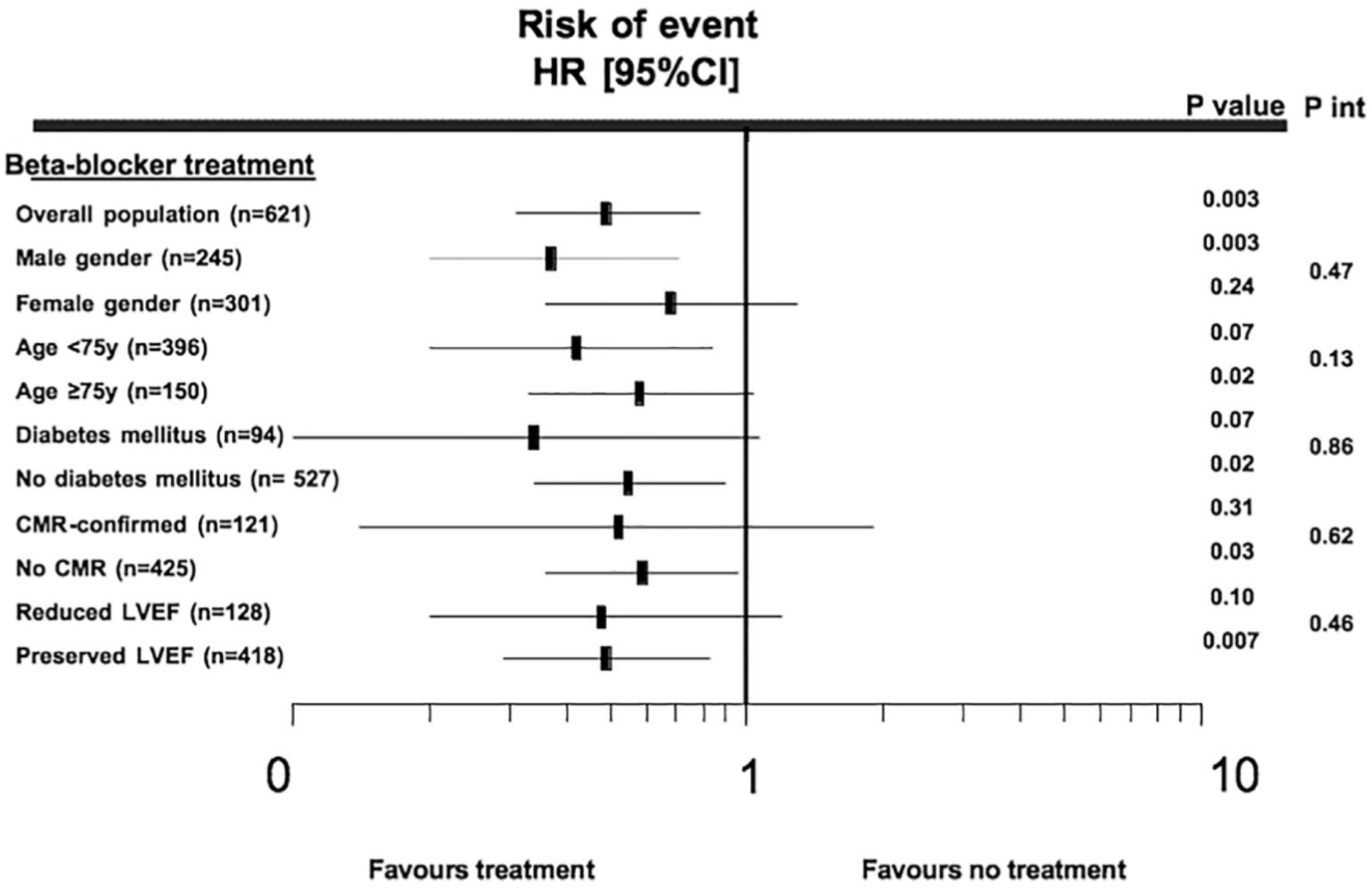
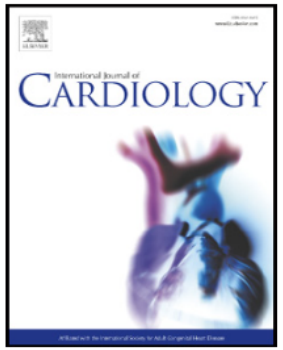


Fig. 2. Forest plot analysis for the risk of the combined primary endpoint (PE) in major higher risk subsets of patients according to the use of acetylsalicylic acid (ASA) and beta-blockers.



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5. Conclusion

In this multicentre registry, enrolling all consecutive patients with a diagnosis of MINOCA, beta-blockers emerged as significantly associated to a reduced risk of mortality and major cardiovascular events, whereas antiplatelet drugs, used as single or dual therapy did not demonstrate beneficial effects on the PE, displaying even a potentially harmful impact on clinical outcomes. Therefore, patients with MINOCA should be considered as a unique subset of acute coronary syndrome patients, in whom the conventional pharmacological strategies recommended for CAD-related ACS could prove ineffective.

Therefore, an adequate diagnostic assessment, carefully characterizing the pathogenic mechanisms and a selection of more targeted treatments is needed in order to improve clinical outcomes. Future large-scale studies are necessary to provide more defined indications on the best therapeutic approach to MINOCA.