

Anticoagulation for the treatment of left ventricular thrombus in patients with acute myocardial infarction and renal impairment

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Introduction Left ventricular thrombus (LVT) formation is one of the devastating sequelae of acute myocardial infarction (AMI) due to potential embolic complications such as ischemic stroke.¹ Current guidelines recommend oral anticoagulation in addition to dual antiplatelet therapy (DAPT) for the treatment of post-AMI LVT, but this is associated with an increased risk of bleeding.²⁻⁴ Patients with AMI share comorbidities with patients with chronic kidney disease (CKD). Patients with CKD are predisposed to atherothrombotic and thromboembolic complications and increased bleeding risk.^{5,6} Therefore, the use of anticoagulation in patients with CKD requires the clinician to balance the risk of thromboembolism and bleeding.⁶ This study aims to compare the clinical characteristics and outcomes of AMI patients with LVT based on the presence of renal impairment.

Methods This was a retrospective, single-center, observational study performed at a tertiary academic medical center. Ethics approval was obtained from the local institutional review board (2013/00442) with a waiver of patient consent. Supplementary material, *Figure S1* shows the patient selection process, stratified by the presence or absence of renal impairment. We collected baseline clinical characteristics as well as treatment and outcomes data.

Routine laboratory tests including a full blood count and renal panel were performed on admission. Patients with renal impairment were identified based on an estimated glomerular filtration rate (eGFR) of less than 60 ml/min/1.73 m². All patients diagnosed with AMI were treated according to our institution's protocol. Patients were treated with DAPT and coronary revascularization

unless contraindicated or if the patient declined treatment.² All patients underwent echocardiogram (transthoracic echocardiography) within one week of admission and oral anticoagulation was initiated in those found with LVT. Anticoagulation was initiated with warfarin and heparin bridging, targeting a therapeutic international normalized ratio (INR) range of 2 to 3. Triple therapy was defined as the combination of DAPT and oral anticoagulation. Follow-up transthoracic echocardiography was done at an interval of 3 to 6 months to assess for LVT resolution.

Statistical analysis We performed statistical analyses using the *t* test for independent samples for normally distributed continuous variables, the Mann-Whitney test for nonnormally distributed continuous variables, and the χ^2 test for categorical variables with Bonferroni correction (when applicable). Kaplan-Meier analysis with the log-rank test was used for survival analysis. Continuous variables were presented as mean (SD) if they were normally distributed, as median and interquartile range (IQR) if they were not normally distributed, and categorical variables were presented as frequency (proportion). We performed Cox proportional hazards regression analysis to identify independent predictors of thrombus resolution, ischemic stroke, and all-cause mortality. These results were presented as hazard ratios (HRs) and the associated 95% CIs. All *P* values of less than 0.05 were considered statistically significant. Analyses were performed with SPSS, version 24 (IBM Corp, Armonk, New York, United States).

Results A total of 170 patients with AMI and LVT were included, with a rate of loss to follow-up

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of 11% (n = 19) (TABLE 1, Supplementary material, Table S1). The median (IQR) follow-up time for the study cohort was 1.4 (0.3–2.6) years while the total follow-up time was 290 patient-years. Renal impairment (eGFR <60 ml/min/1.73 m²) was present in 25.9% of patients (n = 44). Compared with LVT patients without renal impairment, these patients were older (mean [SD], 69.3 [10.9] years vs 55.9 [12.0] years; $P < 0.001$) and had more cardiovascular risk factors including hypertension ($P = 0.009$), dyslipidemia ($P = 0.04$), and previous stroke or transient ischemic attack (TIA) ($P = 0.03$). A greater proportion of patients with renal impairment had non-ST-segment elevation myocardial infarction (40.9% vs 19.8%; $P = 0.006$) and lower left ventricular ejection fraction (mean [SD], 28.8% [9.8%] vs 35.8% [10.3%]; $P < 0.001$). Fewer LVT patients with renal impairment underwent percutaneous coronary intervention (52.3% vs 72.2%; $P = 0.02$) or were treated with triple therapy for LVT (48.6% vs 72.4%; $P = 0.008$). One patient without renal impairment was treated with a non-vitamin K antagonist oral anticoagulant (NOAC). In terms of outcomes, fewer patients with renal impairment achieved thrombus resolution (40.5% vs 74.3%; $P < 0.001$) while the rate of mortality was higher (59.5% vs 17.6%; $P < 0.001$) compared with those without renal impairment. The incidence of bleeding was similar, even after stratification by antithrombotic strategy (Supplementary material, Table S2).

In the Kaplan–Meier analysis, the cumulative survival in patients with post-AMI LVT and renal impairment was lower compared with those without renal impairment by log-rank test ($P < 0.001$) (Supplementary material, Figure S2). The cumulative hazard of thrombus resolution ($P = 0.63$), stroke ($P = 0.34$), and bleeding events ($P = 0.47$) was similar (Supplementary material, Figures S3–S5).

Older age ($P < 0.001$), previous stroke/TIA ($P < 0.001$), ischemic heart disease ($P = 0.02$), renal impairment ($P < 0.001$), percutaneous coronary intervention use ($P = 0.001$), and absence of anticoagulation ($P < 0.001$) were associated with all-cause mortality, while left ventricular ejection fraction was protective against all-cause mortality in the univariable Cox regression analysis (Supplementary material, Table S3). In the multivariable model that did not include anticoagulation as a variable, renal impairment (HR, 2.46; 95% CI, 1.25–4.84; $P = 0.009$) was an independent predictor of mortality while left ventricular ejection fraction (per 10%) was associated with reduced mortality (HR, 0.44; 95% CI, 0.31–0.64; $P < 0.001$). In the multivariable model including anticoagulation use as a variable, stroke/TIA (HR, 2.93; 95% CI, 1.26–6.82; $P = 0.01$) and ischemic heart disease (HR, 2.30; 95% CI, 1.03–5.16; $P = 0.04$) were associated with greater mortality, while anticoagulation (HR, 0.13; 95% CI, 0.05–0.37; $P < 0.001$) and left ventricular ejection fraction (per 10%) (HR, 0.46; 95% CI, 0.29–0.75;

$P = 0.002$) were found to be protective against all-cause mortality. Consistent with the Kaplan–Meier analysis, renal impairment was not a significant predictor of thrombus resolution or stroke events (Supplementary material, Tables S4 and S5).

Discussion Renal impairment is a risk factor in the development and progression of cardiovascular disease.⁷ In this cohort of patients with post-AMI LVT, we report that a considerable proportion of patients had concomitant renal impairment (25.9%, n = 44/170). Unsurprisingly, this group of patients had a greater prevalence of cardiovascular comorbidities including hypertension, dyslipidemia, and previous stroke or TIA. Furthermore, patients with renal impairment had worse cardiac function with significantly lower left ventricular ejection fraction, and fewer received recommended reperfusion treatment for AMI. Among the post-AMI LVT patients, all-cause mortality was significantly greater in those with renal dysfunction compared with those without (59.5% vs 17.6%), with renal impairment being an independent predictor of mortality.

One possible explanation of these poorer outcomes is that these patients are in a hyperinflammatory and prothrombotic state. Renal impairment reduces clearance of inflammatory substances which may further exacerbate this state.⁸ Hence, eGFR or renal impairment may be useful as a prognostic marker to risk stratify patients with post-AMI LVT, and those with concomitant renal impairment may benefit from a focus on recovery of renal function.

The use of anticoagulation in CKD is often challenging as these patients are concurrently at the risk of thrombotic and bleeding episodes due to alterations in the coagulation pathways.⁹ In patients with CKD and atrial fibrillation, the use of warfarin markedly reduces the risk of stroke, but an unfavorable risk-benefit profile is seen in end-stage renal failure with minimal effect on risk of stroke and increased risk of major bleeding.¹⁰ Based on contemporary guidelines, management of AMI LVT involves oral anticoagulation with concomitant antiplatelet therapy (ie, triple therapy).² However, fewer patients with renal impairment were treated with triple therapy (48.6% vs 72.4%) in this study. Renal impairment was not found to be associated with mortality after adjusting for anticoagulation use. In fact, anticoagulation use was a negative predictor of mortality (HR, 0.13; 95% CI, 0.05–0.37; $P < 0.001$) and hence should be considered in this population of patients. In patients with atrial fibrillation, NOACs have been shown to be at least as efficacious as warfarin in stroke risk reduction whilst having a better bleeding profile; and evidence for their use in patients with advanced CKD is also increasing.¹¹ Further studies are needed to evaluate the role of NOACs in patients with LVT and renal impairment.¹²

TABLE 1 Clinical characteristics of patients with acute myocardial infarction and left ventricular thrombus with or without renal impairment (n = 170)

Variable		With renal impairment (n = 44)	Without renal impairment (n = 126)	P value
Age, y, mean (SD)		69.3 (10.9)	55.9 (12.0)	<0.001
Male gender		36 (81.8)	113 (89.7)	0.17
Comorbidities				
Current or past smoking		15 (34.1)	82 (65.1)	<0.001
Atrial fibrillation		12 (27.3)	12 (9.5)	0.004
Hypertension		30 (68.2)	57 (45.2)	0.009
Dyslipidemia		28 (63.6)	57 (45.2)	0.04
Diabetes mellitus		20 (45.5)	50 (39.7)	0.50
Known IHD		12 (27.3)	20 (15.9)	0.10
Chronic heart failure		8 (18.2)	13 (10.3)	0.17
Stroke/TIA		12 (27.3)	16 (12.7)	0.03
Chronic kidney disease		24 (54.5)	0	<0.001
eGFR ^a , ml/min/1.73 m ² , mean (SD)		38.9 (13.6)	89.7 (13.2)	<0.001
Treatment				
Underwent PCI		23 (52.3)	91 (72.2)	0.02
Antithrombotic therapy strategies (n = 158)	All	–	–	0.02
	None	2 (5.7)	2 (1.6)	>0.99
	Anticoagulation alone	4 (11.4)	5 (4.1)	0.58
	DAPT alone	3 (8.6)	1 (0.8)	0.06
	Anticoagulation + SAPT	9 (25.7)	25 (20.3)	>0.99
	Anticoagulation + DAPT	17 (48.6)	89 (72.4)	0.049
Outcomes				
Thrombus resolution (n = 151)		17 (40.5)	81 (74.3)	<0.001
BARC bleeding (n = 151)	All	–	–	0.30
	Type 0	35 (83.3)	91 (83.5)	>0.99
	Type 1	0	4 (3.7)	0.83
	Type 2	3 (7.1)	10 (9.2)	>0.99
	Type 3	4 (9.5)	4 (3.7)	0.60
Stroke/TIA (n = 154)		6 (14.3)	13 (11.6)	0.65
Mortality (n = 150)		25 (59.5)	19 (17.6)	<0.001

Data are presented as number (percentage) unless otherwise indicated.

a Reference range >60 ml/min/1.73 m²

Abbreviations: BARC, Bleeding Academic Research Consortium; DAPT, dual antiplatelet therapy; eGFR, estimated glomerular filtration rate; IHD, ischemic heart disease; PCI, percutaneous coronary intervention; SAPT, single antiplatelet therapy; TIA, transient ischemic attack

The limitations of our study are as follows. Firstly, given the nature of a retrospective cohort study, we could only describe associations but were unable to establish causation. Secondly, a proportion of patients were lost to follow-up (n = 33, 11.4%) which may affect the generalizability of the results. Lastly, the number of patients with LVT and renal impairment was small, hence it was not feasible to investigate for a graded association between worsening eGFR and outcomes.

Conclusions Higher mortality is observed in patients with post-AMI LVT and renal impairment. While the use of anticoagulation may mitigate this risk, it is underutilized and is challenging

in this patient subgroup. Randomized trials are necessary to determine the optimal antithrombotic treatment strategy for AMI with concomitant LVT and renal impairment.

SUPPLEMENTARY MATERIAL

Supplementary material is available at www.mp.pl/paim.

ARTICLE INFORMATION

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CONFLICT OF INTEREST None declared.

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