TCTAP 2024
The Association Between Free Fatty Acid and Adverse Outcomes in Patients Undergoing Percutaneous Coronary Intervention With or Without Diabetes Mellitus: A Single-Center Cohort Study.

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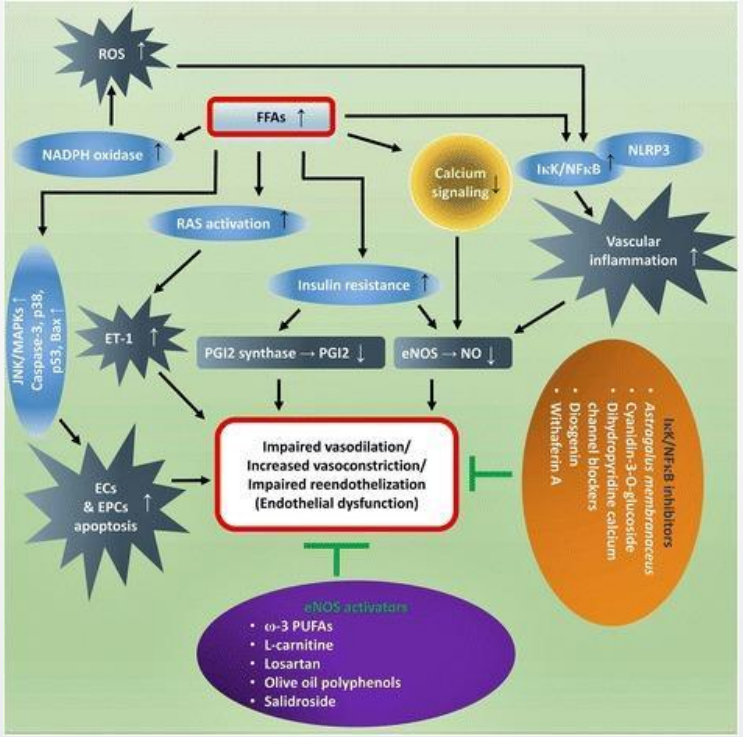
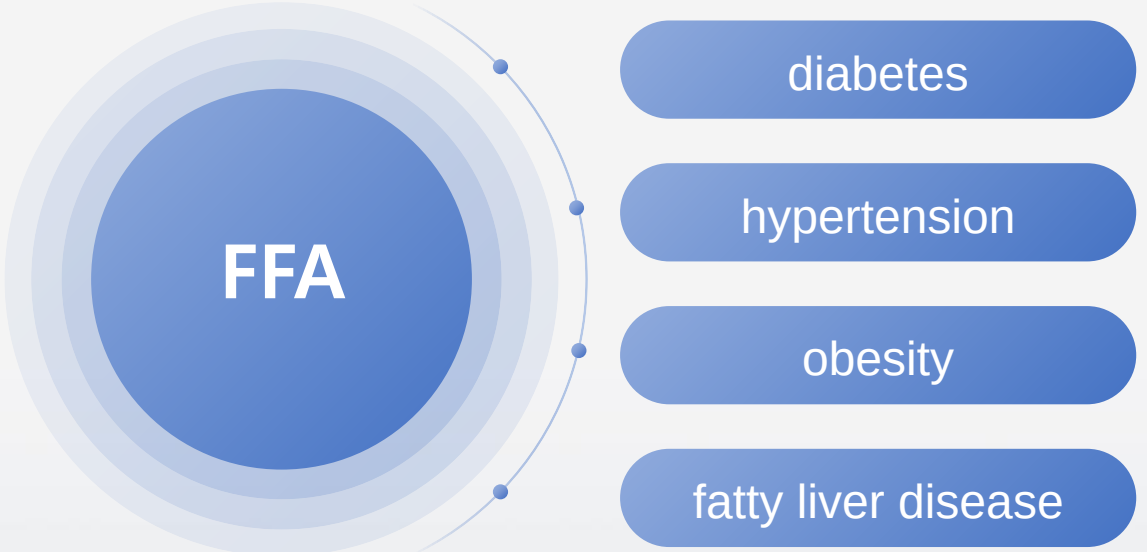
Background

- Free fatty acids (FFA) are released from adipose tissue by triglyceride lipolysis and provide 70% of the energy required by myocardial metabolism.
- Previous studies have indicated that FFA can induce endothelial dysfunction and play a role in the development of atherosclerosis.
- Increased plasma FFA levels have been observed in some metabolic diseases associated with a high risk of coronary artery disease (CAD).



J Biomed Sci. 2017 Jul 27;24(1):50.

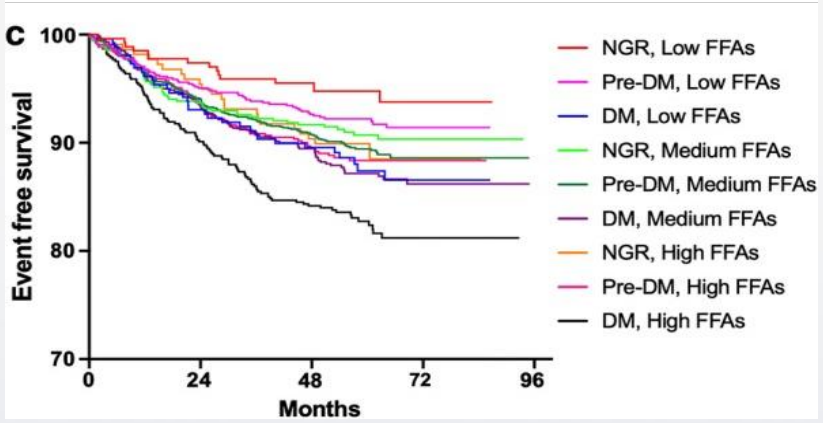


Nutrients. 2021 Jul 28;13(8):2590.

Background

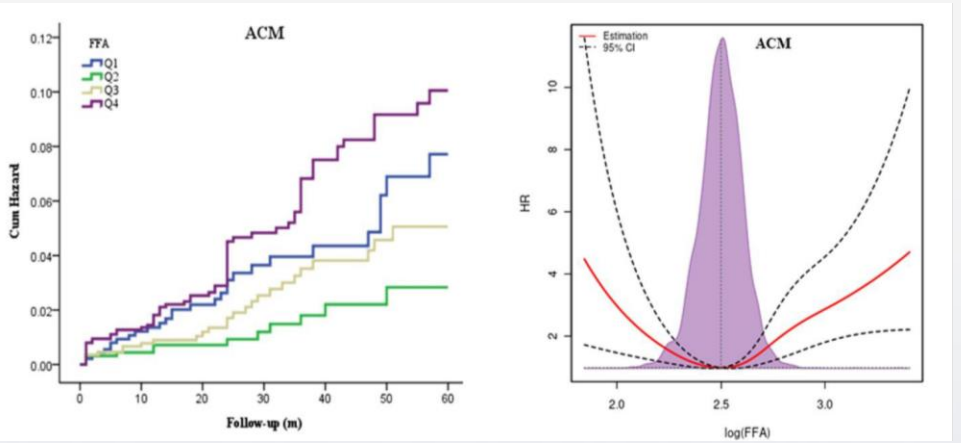
However, research on the relationship between FFA and adverse outcomes in CAD patients with different diabetes statuses is currently limited and controversial.

FFAs	HR (95% CI)		
	Events/subjects 608/5433	Crude Model	Adjusted Model
NGR			
Low FFAs	15/268	Ref	Ref
Medium FFAs	51/553	1.665 (0.936–2.962)	1.543 (0.865–2.752)
High FFAs	23/218	1.925 (1.004–3.689)*	1.856 (0.968–3.559)
Pre-DM			
Low FFAs	61/747	1.457 (0.828–2.563)	1.271 (0.721–2.242)
Medium FFAs	154/1430	1.936 (1.140–3.290)*	1.736 (1.018–2.959)*
High FFAs	70/611	2.098 (1.201–3.664)*	1.779 (1.012–3.126)*
DM			
Low FFAs	32/259	2.245 (1.216–4.145)*	1.937 (1.044–3.594)*
Medium FFAs	96/740	2.354 (1.366–4.056)*	2.017 (1.164–3.494)*
High FFAs	106/607	3.308 (1.926–5.680)*	2.795 (1.619–4.824)*



Cardiovasc Diabetol. 2019; 18: 134.

Variables	Q1		Q2		Q3		Q4	
	HR (95% CI)	*P value*	HR (95% CI)	*P value*	HR (95% CI)	*P value*	HR (95% CI)	*P value*
Individuals with T2DM (n = 4375)								
ACM	2.055 (0.965–4.376)	0.062	Ref	/	1.803 (0.852–3.817)	0.124	3.628 (1.833–7.179)	**<0.001**
CM	2.055 (0.926–4.558)	0.076	Ref	/	1.156 (0.493–2.711)	0.740	3.039 (1.466–6.298)	**0.003**
MACE	1.690 (1.202–2.376)	**0.003**	1.215 (0.843–1.751)	0.297	Ref	/	1.586 (1.152–2.183)	**0.005**
MACCE	1.515 (1.093–2.098)	**0.013**	1.092 (0.769–1.549)	0.624	Ref	/	1.421 (1.049–1.925)	**0.023**
Individuals without T2DM (n = 6020)								
ACM	0.696 (0.340–1.423)	0.321	Ref	/	0.816 (0.410–1.622)	0.561	1.825 (0.986–3.376)	0.055
CM	0.669 (0.268–1.669)	0.389	Ref	/	0.785 (0.324–1.902)	0.593	2.214 (1.031–4.756)	**0.042**
MACE	1.311 (0.950–1.808)	0.099	1.075 (0.766–1.511)	0.675	Ref	/	1.025 (0.720–1.459)	0.893
MACCE	1.231 (0.912–1.663)	0.175	1.060 (0.774–1.451)	0.717	Ref	/	1.106 (0.805–1.520)	0.535



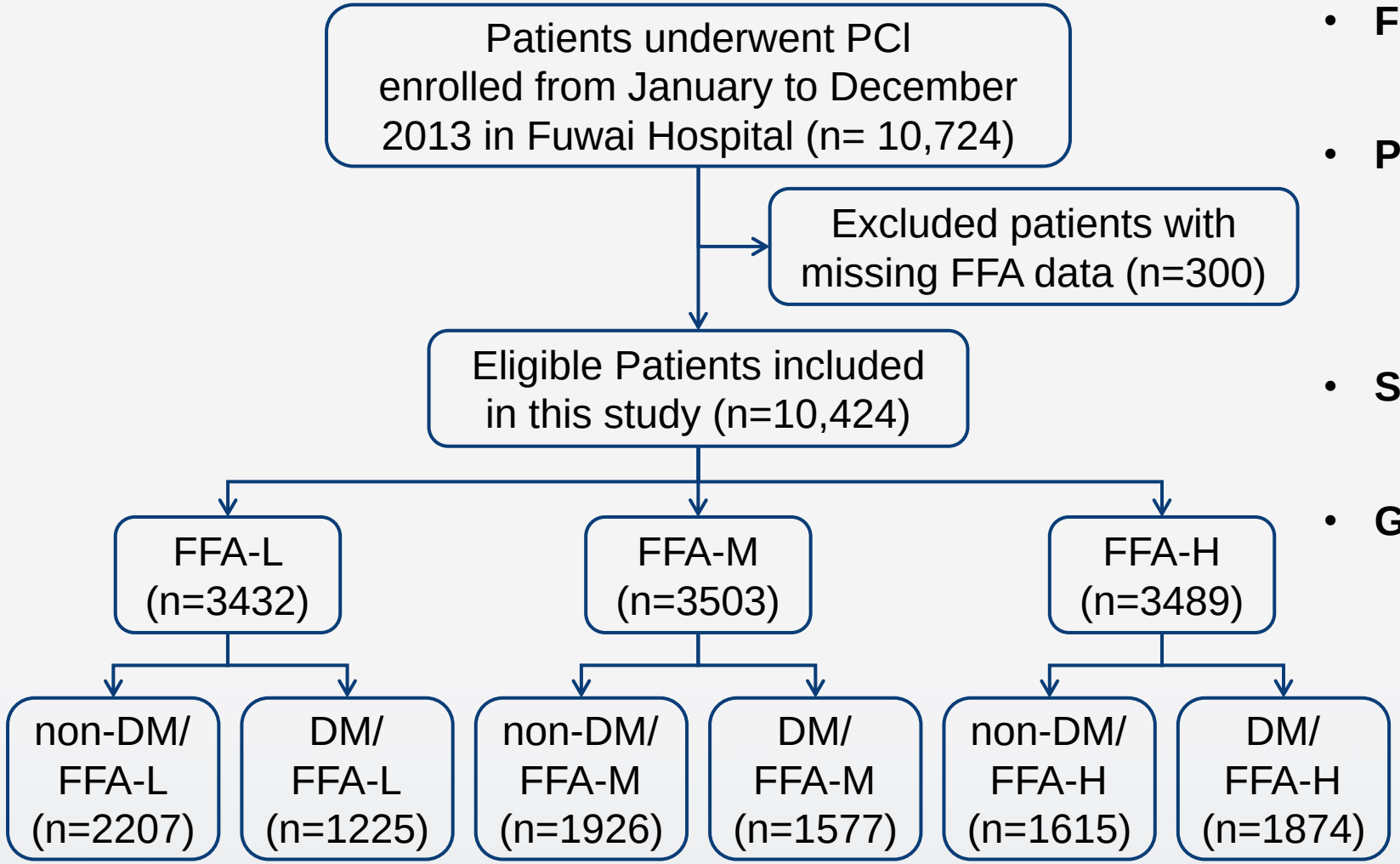
Eur J Prev Cardiol. 2023 Jun 1;30(8):730-739.

Background

Aim：

Our study aimed to investigate the correlation between free fatty acids (FFA) and adverse outcomes in patients with coronary artery disease and different diabetes statuses through a larger sample size and longer follow-up duration.

Methods



- **Follow-up**:

  5 years

- **Primary endpoint:**

  MACCE (a composite of all-cause death, non-fatal myocardial infarction, and non-fatal stroke)

- **Secondary endpoints:**

  The components of MACCE

- **Grouping criteria:**

  FFA-L (FFA < 320 μmol/L)

  FFA-M (320 μmol/L ≤ FFA < 480 μmol/L)

  FFA-H (FFA ≥ 480 μmol/L)

Results

	FFA-L (n=3432)	FFA-M (n=3503)	FFA-H (n=3489)	P value
Demographic characteristics				
Age, yrs	58.18 ± 10.06	57.86 ± 10.31	59.02 ± 10.43	<0.001
Male, %	2752 (80.2)	2774 (79.2)	2519 (72.2)	<0.001
BMI, kg/m2	25.31 ± 3.00	26.18 ± 3.13	26.31 ± 3.32	<0.001
Clinical presentation				0.003
CCS, %	1413 (41.2)	1446 (41.3)	1317 (37.7)	
ACS, %	2019 (58.8)	2057 (58.7)	2172 (62.3)	
Coexisting conditions				
Prior MI, %	684 (19.9)	701 (20.0)	614 (17.6)	0.015
Prior PCI, %	792 (23.1)	885 (25.3)	878 (25.2)	0.058
Prior CABG, %	127 (3.7)	145 (4.1)	152 (4.4)	0.372
Prior stroke, %	391 (11.4)	369 (10.5)	350 (10.0)	0.179
CAD family history, %	794a (23.1)	853a (24.4)	933 (26.8)	0.002
Diabetes, %	1225 (35.7)	1577 (45.0)	1874 (53.7)	<0.001
Hypertension, %	2006 (58.4)	2303 (65.7)	2404 (68.9)	<0.001
Current smoker, %	2066 (60.2)	2068 (59.0)	1817 (52.1)	<0.001
SYNTAX score	11.59 ± 8.10	11.44 ± 7.99	12.07 ± 8.25	0.003
LM/TVD, %	1459 (42.5)	1552 (44.3)	1636 (46.9)	0.001
Number of stents	1.8 ± 1.1	1.8 ± 1.1	1.8 ± 1.1	0.147

Baseline characteristics in patients with high FFA levels:

- Older, female, and higher BMI.
- Higher prevalence of ACS, prior MI, smoking, and comorbidities (including diabetes and hypertension).
- More likely to develop complex coronary artery disease.

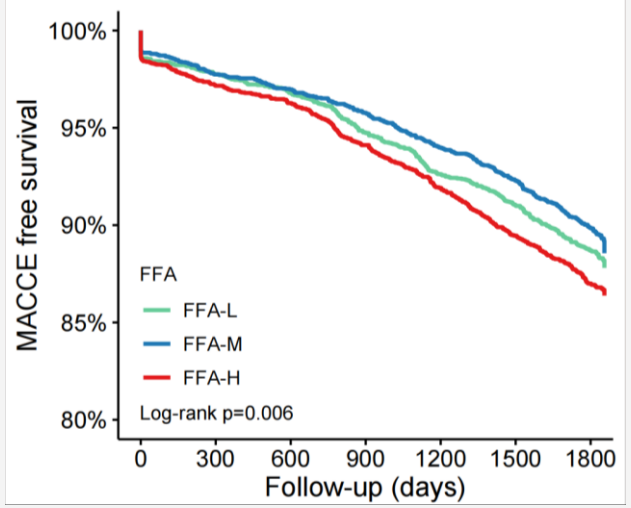
Results

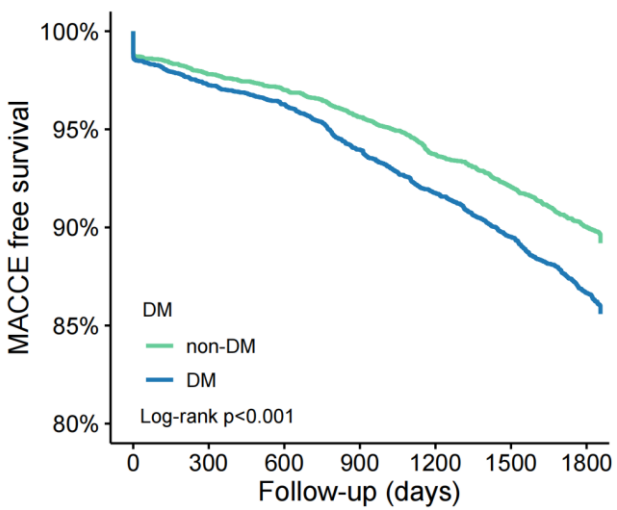
	FFA-L (n=3432)	FFA-M (n=3503)	FFA-H (n=3489)	P value
Laboratory measurements				
FFA, μmol/l	222.82 ± 64.99	391.28 ± 45.81	670.67 ± 232.38	<0.001
TG, mmol/l	1.59 ± 0.84	1.83 ± 1.03	1.93 ± 1.30	<0.001
LDL-C, mmol/l	2.40 ± 0.86	2.48 ± 0.90	2.63 ± 0.96	<0.001
HDL-C, mmol/l	1.02 ± 0.26	1.00 ± 0.27	1.08 ± 0.30	<0.001
FBG, mmol/L	5.73 ± 1.73	6.07 ± 1.93	6.71 ± 2.40	<0.001
HbA1c, %	6.42 ± 1.09	6.62 ± 1.22	6.80 ± 1.34	<0.001
Albumin, g/l	41.74 ± 3.78	42.82 ± 3.97	44.01 ± 4.06	<0.001
eGFR, ml/min/1.73m²	92.08 ± 14.48	92.09 ± 14.80	90.03 ± 15.80	<0.001
hsCRP, mg/l	2.81 ± 3.51	3.19 ± 3.77	3.70 ± 4.13	<0.001
LVEF, %	63.14 ± 6.91	62.91 ± 7.18	62.39 ± 7.59	<0.001
Medication at discharge				
Aspirin, %	3393 (98.9)	3461 (98.8)	3440 (98.6)	0.574
Clopidogrel, %	3376 (98.4)	3448 (98.4)	3446 (98.8)	0.332
CCB, %	1592 (46.4)	1664 (47.5)	1818 (52.1)	<0.001
β-blocker, %	3067 (89.4)	3162 (90.3)	3177 (91.1)	0.060
Statin, %	3291 (95.9)	3375 (96.3)	3335 (95.6)	0.269

Baseline characteristics in patients with high FFA levels:

- Higher levels of blood lipids, glucose, Albumin, and hsCRP.
- More likely to receive calcium channel blocker at discharge.

Results



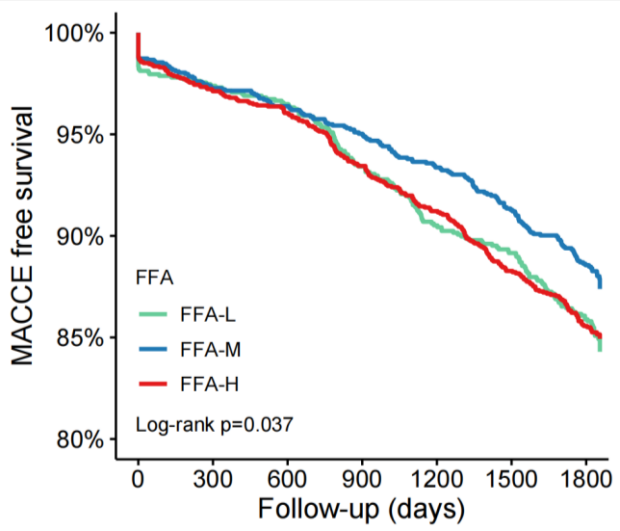


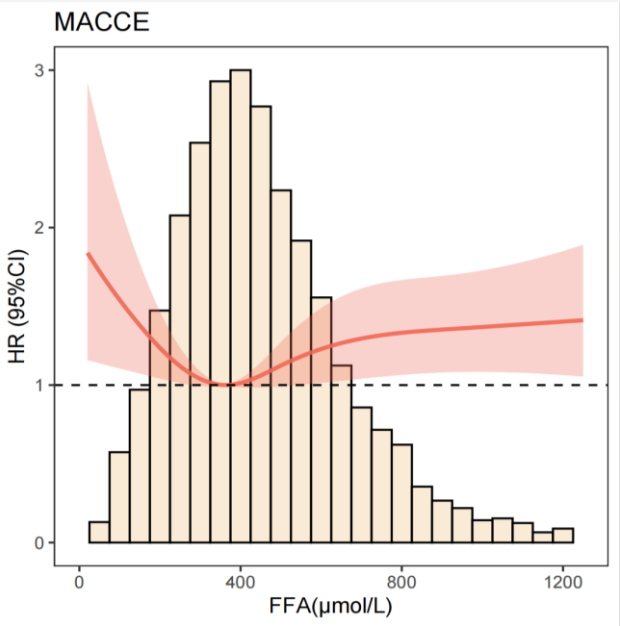
- The association between FFA and the risk of MACCE was "**U-shaped**" in patients undergoing PCI , with patients in the FFA-M group having the lowest risk of MACCE and the FFA-H group having the highest risk of MACCE.
- Diabetic patients had a significantly higher risk of MACCE compared to non-diabetic patients.

	Event/total (%)	Crude HR (95%CI)	P value	Adjusted HR (95%CI)	P value
FFA					
FFA-L	386/3432 (11.2)	1.094 (0.948-1.262)	0.221	1.109 (0.959-1.283)	0.163
FFA-M	362/3503 (10.3)	Ref	-	Ref	-
FFA-H	443/3489 (12.7)	1.250 (1.088-1.437)	**0.002**	1.213 (1.053-1.398)	**0.008**
Diabetes status					
Non-DM	570/5748 (9.9)	Ref	-	Ref	-
DM	621/4676 (13.3)	1.366 (1.219-1.531)	**<0.001**	1.179 (1.048-1.327)	**0.006**

*The multivariable Cox regression analysis adjusted for age, sex, BMI, smoking status, prior MI, prior PCI, prior CABG, prior stroke, hypertension, CAD family history, LM/TVD, LVEF, eGFR, LDL, albumin, hsCRP, CCB at discharge.

Results



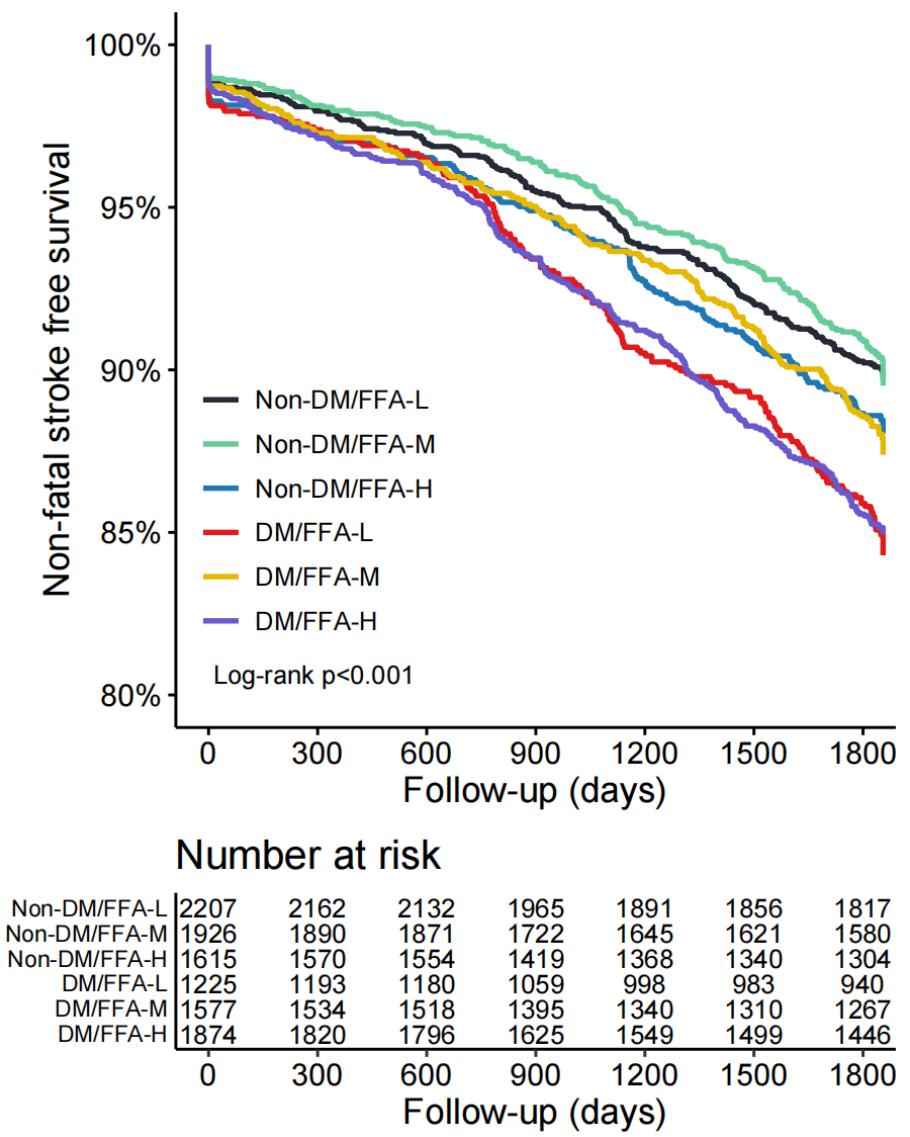


- Subgroup analysis according to diabetes status revealed that this U-shaped relationship is more significant among diabetic patients, while it is not significant among non-diabetic patients.
- Restricted cubic spline analysis indicated that the FFA level of 362 μmol/L is associated with the lowest risk of MACCE in diabetic patients.

	Event/total (%)	Crude HR (95%CI)	P value	Adjusted HR (95%CI)	P value
Patients with DM					
FFA-L	175/1225 (14.3)	1.263 (1.027-1.555)	**0.027**	1.250 (1.013-1.543)	**0.037**
FFA-M	182/1577 (11.5)	Ref	-	Ref	-
FFA-H	264/1874 (14.1)	1.246 (1.032-1.505)	**0.022**	1.251 (1.032-1.516)	**0.023**
Patients without DM					
FFA-L	211/2207 (9.6)	1.020 (0.836-1.245)	0.844	1.020 (0.833-1.249)	0.846
FFA-M	180/1926 (9.3)	Ref	-	Ref	-
FFA-H	179/1615 (11.1)	1.200 (0.976-1.476)	0.084	1.148 (0.928-1.419)	0.203

*models were adjusted for age, sex, BMI, smoking status, prior MI, prior PCI, prior CABG, prior stroke, hypertension, CAD family history, LM/TVD, LVEF, eGFR, LDL, albumin, hsCRP, CCB at discharge.

Results



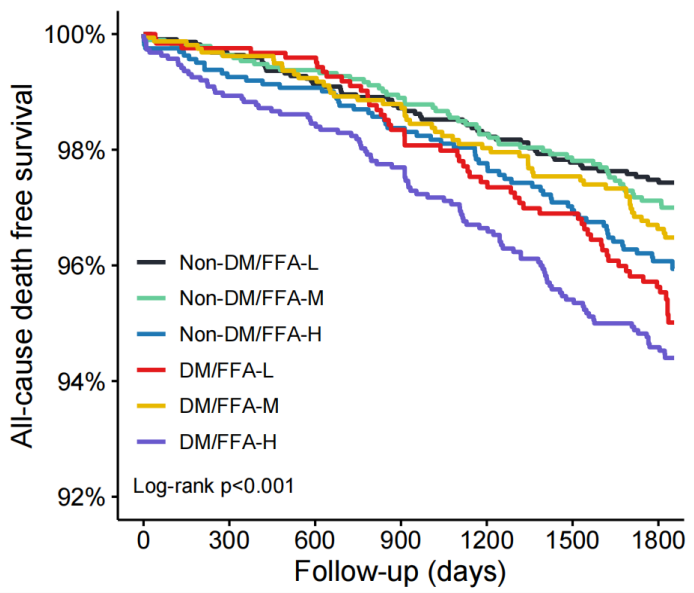
Patients were further grouped based on FFA and diabetes status:

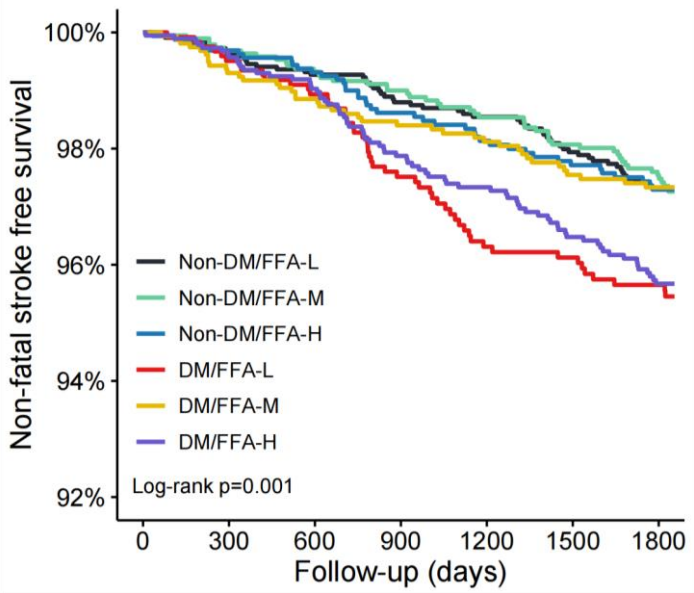
- Patients in the DM/FFA-L and DM/FFA-H groups exhibited a significant higher risk of MACCE compared to non-DM/FFA-L group.

	Event/total (%)	Adjusted HR (95%CI)	P value
Non-DM/FFA-L	211/2207 (9.6)	Ref	-
Non-DM/FFA-M	180/1926 (9.3)	0.992 (0.812-1.212)	0.939
Non-DM/FFA-H	179/1615 (11.1)	1.185 (0.965-1.454)	0.106
DM/FFA-L	175/1225 (14.3)	1.375 (1.123-1.683)	**0.002**
DM/FFA-M	182/1577 (11.5)	1.075 (0.878-1.317)	0.482
DM/FFA-H	264/1874 (14.1)	1.308 (1.080-1.584)	**0.006**

*models were adjusted for age, sex, BMI, smoking status, prior MI, prior PCI, prior CABG, prior stroke, hypertension, CAD family history, LM/TVD, LVEF, eGFR, LDL, albumin, hsCRP, CCB at discharge.

Results





Analysis of the secondary endpoints:

- Compared to the non-DM/FFA-L group, the DM/FFA-L and DM/FFA-H groups had a significantly higher risk of all-cause death and non-fatal stroke, while non-DM/FFA-H group had a significantly higher risk of all-cause death.

	All-cause death		Non-fatal stroke	
	Adjusted HR (95%CI)	**P value**	**Adjusted HR (95%CI)**	**P value**
Non-DM/FFA-L	Ref	-	Ref	-
Non-DM/FFA-M	1.224 (0.838-1.790)	0.296	1.055 (0.714-1.559)	0.787
Non-DM/FFA-H	1.647 (1.131-2.400)	**0.009**	1.077 (0.710-1.633)	0.728
DM/FFA-L	1.568 (1.073-2.292)	**0.020**	1.564 (1.067-2.293)	**0.022**
DM/FFA-M	1.177 (0.799-1.735)	0.410	0.956 (0.632-1.448)	0.833
DM/FFA-H	1.882 (1.326-2.670)	**<0.001**	1.505 (1.041-2.177)	**0.030**

*models were adjusted for age, sex, BMI, smoking status, prior MI, prior PCI, prior CABG, prior stroke, hypertension, CAD family history, LM/TVD, LVEF, eGFR, LDL, albumin, hsCRP, CCB at discharge.

Conclusion

- Both elevated and diminished levels of FFA are significantly associated with a higher risk of major adverse events in diabetic patients undergoing PCI. However, this relationship is attenuated in non-diabetic patients.
- FFA is a potential risk-stratifying biomarker that may help identify high-risk individuals among diabetic patients undergoing PCI.

Disclosure

- There is no potential conflict of interest to disclose.