

Table S1 Obtained GWAS data for DECRs-related proteins

Genes	Protein Coding	GWAS resource				
		Year	Case	SNPs	Population	PMID
MAPK14	Mitogen-activated protein kinase 14	2017	-	501,428	European	28240269 ¹
CD55	DAF					
CLU	Clusterin					
TFPI	Tissue factor pathway inhibitor					
PROS1	Protein S					
	Carcinoembryonic antigen-related cell adhesion	2018	3301	10,534,735	European	29875488 ²
CEACAM1	molecule 1					
FYN	FYN Proto-Oncogene, Src Family Tyrosine Kinase					
	Phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic					
	subunit alpha isoform:Phosphatidylinositol 3-kinase					
PIK3R1	regulatory subunit alpha complex	2020	1301	18,166,693	European	33303764 ³
ENTPD1	Ectonucleoside Triphosphate Diphosphohydrolase 1					
F8	Coagulation Factor VIII					
MERTK	Tyrosine-protein kinase Mer levels					
CD40LG	CD40 Ligand					
F3	Tissue factor levels					

DAF: decay accelerating factor; SNP: single nucleotide polymorphism; GWAS: Genome-Wide Association Study; PMID: PubMed ID of articles.

1. Suhre K, Arnold M, Bhagwat AM, et al. Connecting genetic risk to disease end points through the human blood plasma proteome. *Nat Commun.*

Feb 27 2017;8:14357. doi:10.1038/ncomms14357

2. Sun BB, Maranville JC, Peters JE, et al. Genomic atlas of the human plasma proteome. *Nature*. Jun 2018;558(7708):73-79. doi:10.1038/s41586-018-0175-2

3. Gilly A, Park YC, Png G, et al. Whole-genome sequencing analysis of the cardiometabolic proteome. *Nat Commun*. Dec 10 2020;11(1):6336. doi:10.1038/s41467-020-20079-2

Table S2 Obtained differentially expressed coagulation-related genes (DECGRs)

DECGRs	Coding Protein	DECGRs	Coding Protein	DECGRs	Coding Protein
CYP4F2	Mitogen-activated protein kinase 14	CEACAM1	Carcinoembryonic antigen-related cell adhesion molecule 1	MASP2	MBL Associated Serine Protease 2
TFPI	Tissue factor pathway inhibitor	RAB27A	Ras-Related Protein Rab-27A	CD40LG	CD40 Ligand
CLU	Clusterin	ITGAM	Integrin Subunit Alpha M	PIK3CB	Phosphatidylinositol-4,5-Bisphosphate 3-Kinase Catalytic Subunit Beta
MAPK14	Mitogen-activated protein kinase 14	CR1	Complement Receptor Type 1	ENTPD1	Ectonucleoside Triphosphate Diphosphohydrolase 1
MERTK	Tyrosine-protein kinase Mer levels	ITPR3	Inositol 1,4,5-Trisphosphate Receptor Type 3	F8	Coagulation Factor VIII
PIK3R1	Phosphoinositide-3-Kinase, Regulatory Subunit 1	FYN	FYN Proto-Oncogene, Src Family Tyrosine Kinase	PABPC4	Poly(A) Binding Protein Cytoplasmic 4
P2RX1	P2X1 Receptor	GNAQ	G Protein Subunit Alpha Q	AK3	Adenylate Kinase 3
PROS1	Protein S	PRKACB	Protein Kinase CAMP-Activated Catalytic Subunit Beta	F3	Tissue factor
CD59	Membrane Attack Complex Inhibition Factor	EMILIN2	Elastin Microfibril Interfacer 2		
CD55	DAF	RASGRP1	RAS Guanyl Releasing Protein 1		

DAF: decay accelerating factor

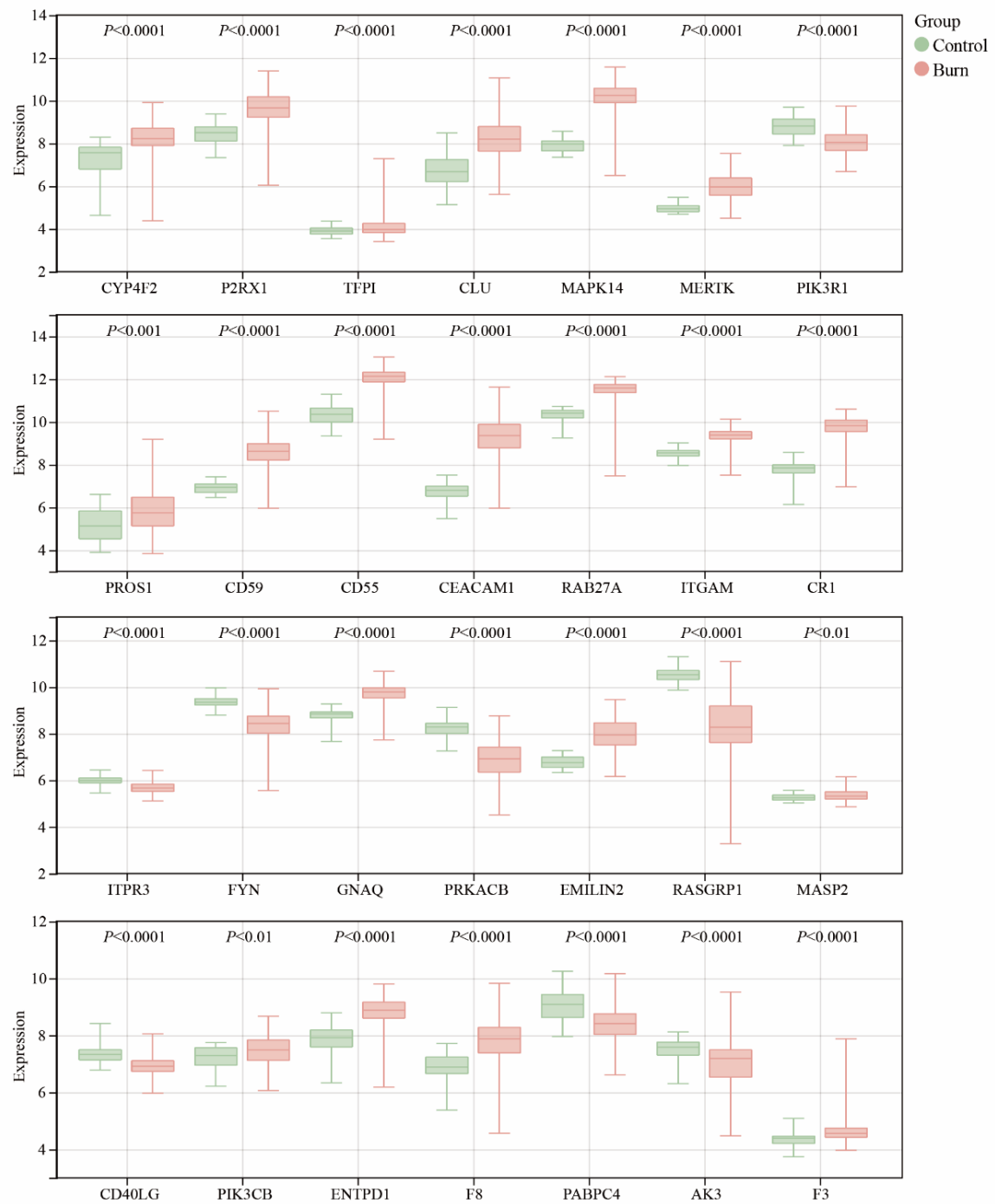


Figure S1. Differential expression of 28DECRGs in GSE37069.

Table S3: MR results and sensitivity analysis

Outcome	MR results						Heterogeneity		Horizontal pleiotropy	
	Method	nSNP	b	SE	P value	OR (95%CI)	Q value	P value	Egger intercept	P value
CD40 ligand levels	Weighted median	18	0.127	0.128	0.321	1.135(0.884-1.459)	14.122	0.049	0.071	0.572
	IVW	18	-0.020	0.090	0.825	0.980(0.821-1.170)				
Carcinoembryonic antigen-related cell adhesion molecule 1	Weighted median	18	-0.020	0.059	0.740	0.981(0.874-1.101)				
	IVW	18	-0.012	0.041	0.769	0.988(0.912-1.071)				
Clusterin	Weighted median	8	-0.177	0.186	0.340	0.838(0.582-1.205)				
	IVW	8	-0.348	0.135	0.010	0.706(0.541-0.920)				
DAF	Weighted median	8	0.407	0.192	0.034	1.502(1.031-2.187)				
	IVW	8	0.181	0.189	0.338	1.199(0.827-1.737)				
Ectonucleoside triphosphate diphosphohydrolase 1	Weighted median	18	-0.030	0.062	0.626	0.970(0.859-1.096)				
	IVW	18	-0.017	0.041	0.680	0.983(0.907-1.065)				
Coagulation Factor VIII	Weighted median	18	0.005	0.056	0.923	1.005(0.900-1.123)				
	IVW	18	-0.002	0.041	0.953	0.998(0.921-1.081)				
Tyrosine-protein kinase Fyn	Weighted median	18	-0.025	0.058	0.674	0.976(0.870-1.094)				
	IVW	18	0.010	0.043	0.809	1.010(0.930-1.098)				
MAPK14	Weighted median	8	-0.078	0.187	0.675	0.925(0.641-1.333)				
	IVW	8	-0.111	0.180	0.539	0.895(0.629-1.275)				
Tyrosine-protein kinase Mer levels	Weighted median	19	-0.028	0.123	0.820	0.972(0.764-1.237)				
	IVW	19	-0.020	0.089	0.821	0.980(0.823-1.167)				

PIK3CA/PIK3R1	Weighted median	8	0.168	0.178	0.345	1.183(0.835-1.675)				
	IVW	8	0.043	0.135	0.750	1.044(0.802-1.359)				
Protein S	Weighted median	8	0.366	0.196	0.062	1.442(0.982-2.117)	7.392	0.389	0.056	0.54
	IVW	8	0.340	0.139	0.015	1.405(1.069-1.845)				
Tissue factor levels	Weighted median	19	-0.332	0.130	0.011	0.718(0.556-0.926)	21.192	0.27	-0.017	0.697
	IVW	19	-0.230	0.097	0.018	0.794(0.657-0.961)				
TFPI	Weighted median	8	0.180	0.171	0.293	1.197(0.856-1.674)	7.427	0.386	0.129	0.150
	IVW	8	0.272	0.136	0.045	1.313(1.007-1.713)				

MR: Mendelian randomization; IVW: Inverse Variance Weighted; DAF: decay accelerating factor; TFPI: tissue factor pathway inhibitor

Table S4: Patient demographics and baseline characteristics

Characteristic	Overall, n = 583¹	Survival, n = 497¹	Death, n = 86¹	<i>P</i>-value²
Sex-male	409 (70%)	345 (69%)	64 (74%)	0.349
Age (year)	48 (36.00, 57.50)	47 (35.00, 56.00)	56 (47.25, 68.00)	<0.001
TBSA (%)	60.0 (44.50, 80.00)	55.0 (40.00, 75.00)	82.5 (61.25, 94.00)	<0.001
Weight (kg)	65.0 (58.00, 72.25)	65.0 (58.00, 72.00)	65.0 (60.00, 73.50)	0.459
Cause				0.294
Fire	479 (82%)	404 (81%)	75 (87%)	
Corrosive injury	19 (3%)	18 (4%)	1 (1%)	
Scald injury	59 (10%)	50 (10%)	9 (10%)	
Electric injury	26 (4%)	25 (5%)	1 (1%)	
Inhalation injury	433 (74%)	377 (76%)	56 (65%)	0.035
Coagulation function				
Prothrombin time (s)	11.7 (11.00, 12.70)	11.6 (11.00, 12.60)	12.3 (11.30, 14.00)	0.002
APTT (s)	27.2 (23.50, 32.50)	27.0 (23.30, 31.60)	31.6 (24.63, 37.80)	0.003
Thrombin time (s)	18.5 (16.90, 20.20)	18.5 (16.90, 20.10)	18.6 (16.63, 20.28)	0.709
D-dimer (mg/L)	2.6 (1.12, 5.94)	2.3 (1.04, 5.25)	5.3 (2.68, 15.32)	<0.001
INR	1.0 (0.93, 1.10)	1.0 (0.93, 1.08)	1.1 (0.97, 1.20)	<0.001
Fibrinogen (g/L)	2.5 (1.98, 3.17)	2.5 (2.00, 3.12)	2.6 (1.94, 3.36)	0.626
Calcium (mmol/L)	2.0 (1.82, 2.19)	2.0 (1.82, 2.19)	2.0 (1.82, 2.17)	0.837

PH	7.4 (7.33, 7.42)	7.4 (7.33, 7.42)	7.4 (7.30, 7.40)	0.034
Lactic acid (mmol/L)	3.8 (2.30, 5.25)	3.5 (2.20, 5.15)	4.5 (3.16, 5.68)	0.001
Liver and kidney function				
Total bilirubin (μmol/L)	17.1 (11.50, 25.25)	16.3 (11.40, 24.20)	20.5 (12.85, 30.53)	0.010
Creatinine (μmol/L)	74.0 (58.00, 93.05)	70.2 (56.00, 88.00)	97.7 (79.63, 147.83)	<0.001
Alkaline phosphatase (U/L)	61.9 (51.00, 72.42)	61.0 (51.00, 72.00)	62.9 (52.25, 73.75)	0.345
Albumin (g/dL)	33.3 (27.30, 38.30)	33.7 (28.30, 38.30)	28.7 (23.33, 36.95)	0.001
Blood cell parameters				
RBC	5.3 (4.79, 5.83)	5.3 (4.79, 5.83)	5.2 (4.75, 5.77)	0.418
WBC	19.9 (14.38, 26.54)	19.2 (14.03, 26.00)	23.3 (16.87, 29.88)	0.002
Platelet (10 ⁹ /L)	238.0 (178.00, 309.50)	234.0 (172.00, 304.00)	264.5 (197.25, 362.50)	0.016
Hemoglobin level (g/L)	161.0 (143.00, 177.00)	161.0 (144.00, 176.00)	164.0 (141.25, 180.75)	0.839
Time post burn (hours)	3.0 (2.00, 6.00)	3.7 (2.00, 6.00)	3.0 (2.00, 5.00)	0.131
Length of stay (days)	36.0 (21.00, 62.00)	40.0 (27.00, 66.00)	9.0 (4.00, 18.00)	<0.001
Anamnesis				
Hypertension	49 (8%)	38 (8%)	11 (13%)	0.112
Diabetes mellitus	19 (3%)	15 (3%)	4 (5%)	0.505
Chronic cardiac disease	7 (1%)	5 (1%)	2 (2%)	0.276
Stroke	9 (2%)	6 (1%)	3 (3%)	0.134
Intervention				

CRRT	21 (4%)	9 (2%)	12 (14%)	<0.001
Anticoagulation	68 (12%)	57 (11%)	11 (13%)	0.724
Mechanical ventilation	225 (39%)	171 (34%)	54 (63%)	<0.001

¹n (%);middle(IQR). ²Pearson's Chi-squared test; Wilcoxon rank sum test; Fisher's exact test

TBSA: total body surface area; APTT: activated partial thromboplastin time; INR: international normalized ratio; TLIB: total bilirubin;
RBC: red blood cell; WBC: white blood cell; CRRT: continuous renal replacement therapy.

Table S5: Variables screened by three algorithms

variables	Univariable		LASSO		stepwise-backward		Elastic Net	
	HR (95%CI)	P value	HR (95%CI)	P value	HR (95%CI)	P value	HR (95%CI)	P value
Age	1.05 (1.03-1.00)	<0.001	-	-	1.05 (1.03-1.06)	<0.001	-	-
TBSA	1.04 (1.03-1.00)	<0.001	1.03 (1.02-1.05)	<0.001	1.04 (1.02-1.05)	<0.001	1.03 (1.02-1.05)	<0.001
Inhalation injury(Yes)	1.57 (1.02-2.50)	0.038	-	-	-	-	-	-
Prothrombin time	1.05 (1.03-1.00)	<0.001	1.07 (1.00-1.14)	0.069	-	-	1.07 (1.00-1.14)	0.063
APTT	1.03 (1.01-1.00)	<0.001	-	-	-	-	-	-
Thrombin time	1.04 (1.00-1.00)	0.064	0.93 (0.87-0.99)	0.029	-	-	0.93 (0.87-0.99)	0.028
D-dimer	1.02 (1.01-1.00)	<0.001	1.02 (1.01-1.03)	0.001	1.01 (1.00-1.02)	0.038	1.02 (1.01-1.03)	0.001
INR	4.09 (1.93-8.00)	<0.001	0.57 (0.16-1.96)	0.372			0.57 (0.16-1.96)	0.352
Fibrinogen	0.94 (0.79-1.90)	0.42	-	-	-	-	-	-
Calcium	1.57 (0.88-2.50)	0.125	2.98 (1.43-6.23)	0.004	3.83 (1.79-8.19)	0.001	2.98 (1.43-6.23)	0.004

PH	0.01 (0.00-0.00)	<0.001	0.35 (0.03-4.37)	0.414	-	-	0.35 (0.03-4.37)	0.382
Lactic acid	1.11 (1.05-1.10)	<0.001	1.04 (0.98-1.11)	0.165	1.08 (1.01-1.14)	0.021	1.04 (0.98-1.11)	0.167
Total bilirubin	1.01 (1.00-1.00)	0.027	1.01 (1.00-1.03)	0.081	1.01 (1.00-1.03)	0.067	1.01 (1.00-1.03)	0.07
Creatinine	1.01 (1.01-1.00)	<0.001	1.01 (1.01-1.02)	<0.001	1.01 (1.01-1.01)	<0.001	1.01 (1.01-1.02)	<0.001
Albumin	0.96 (0.94-0.90)	0.003	0.98 (0.95-1.02)	0.354	0.97 (0.94-1.00)	0.066	0.98 (0.95-1.02)	0.333
WBC	1.03 (1.01-1.00)	0.003	-	-	-	-	-	-
Platelet	1.00 (1.00-1.00)	0.003	1.00 (1.00-1.00)	0.326	-	-	1.00 (1.00-1.00)	0.286

TBSA: total body surface area; APTT: activated partial thromboplastin time; INR: international normalized ratio; WBC: white blood cell

Table S6. Mediation analysis of D-dimer and calcium for the associations between TBSA and death

Mediator	Total effect		Indirect effect		Direct effect		Proportion mediated, % (95% CI)
	Coefficient (95% CI)	<i>P</i> value	Coefficient (95% CI)	<i>P</i> value	Coefficient (95% CI)	<i>P</i> value	
D-dimer	0.00058 (0.00026, 0.00090)	<0.001	0.00002 (0.00000, 0.00007)	0.048	0.00057 (0.00025, 0.00087)	<0.001	2.9 (0.0, 9.4)
Calcium	0.00060 (0.00028, 0.00092)	<0.001	0.00001 (-0.00003, 0.00004)	0.56	0.00060 (0.00027, 0.00090)	<0.001	1.1 (-4.1, 6.1)

Indirect effect: mediation effect of D-dimer or calcium between TBSA and death. Direct effect; association between TBSA and death without mediation. The mediation analyses were adjusted for age, TBSA, inhalation injury, PH, lactic acid, total bilirubin, creatinine, albumin and WBC

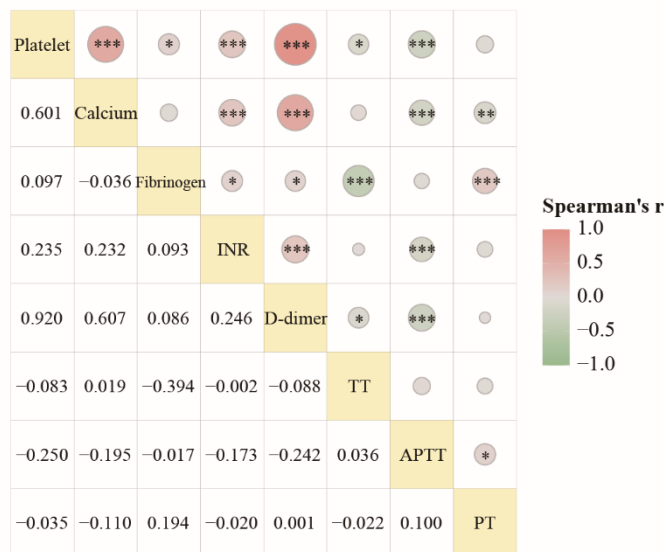


Figure S2 Correlation between coagulation related variables. *: $P < 0.05$; **: $P < 0.01$; ***: $P < 0.001$. INR: international normalized ratio; TT: Thrombin time; APTT: activated partial thromboplastin time; PT: Prothrombin time

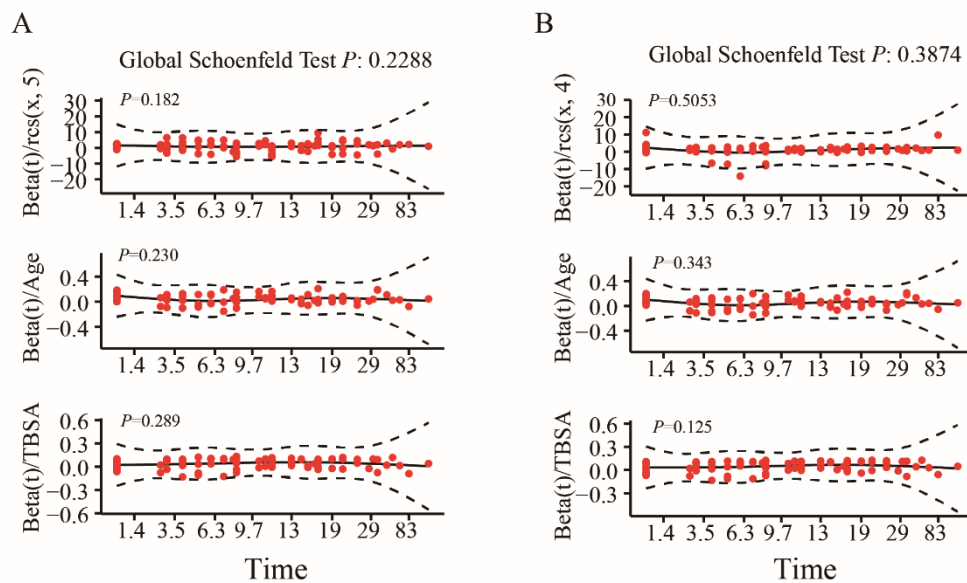


Figure S3. Schoenfeld test for Cox proportional-hazards model. P value > 0.05 indicated that the survival risk does not change over time. The Cox model is considered to be consistent with the proportional risk assumption.