



SCUBE-1 as a novel predictor of thromboembolic event

Hatice Şeyma AKÇA^{ID}

Department of Emergency Medicine, University of Karamanoğlu Mehmet Bey, Karaman Education and Research Hospital, Karaman, Türkiye

Received: 07.12.2022

Accepted/Published Online: 22.01.2023

Final Version: 18.03.2023

Dear Editor,

SCUBE-1 is a newly identified, produced cell surface protein determined through embryogenesis's first part. The protein contains cascading EGF-like repeats following the N-terminal signal peptide sequence, a spacer area, cysteine-rich recurrence motifs, and a CUB domain at the C-terminus. These molecules are collected in alpha granules in inactivated platelets, translocated to the platelet surface after stimulation by thrombin, secreted as small fathomable fragments, and incorporated into the thrombus. After platelet activation, SCUBE-1 expression increases, and SCUBE-1 migrates to the cell surface, cleaves, and is issued into the flow as minor soluble units. These circulating particles increase platelet-platelet bonds and agglutination in thrombotic situations. In addition, it has been shown that it is associated with acute ischemia and an increase in hypertension due to the increase in SCUBE-1 values in endothelial damage. SCUBE-1 accumulation was detected immune-histochemically in the subendothelial matrix of improved atherosclerotic lesions in humans. Platelet stimulation and accumulation are responsible for acute ischemic complications (1-3). It is thought that SCUBE-1 may be a new platelet endothelial adhesion molecule.

There are many findings in the literature investigating SCUBE-1 and thromboembolic events (1-4). For example, Yıldırım et al. described that SCUBE-1 is a marker of platelet activation in cases with ST-elevation myocardial infarction (STEMI) and a novel platelet-endothelial adhesion molecule who experienced primary percutaneous coronary intervention and they recommended that SCUBE-1 can use as a predictor of great thrombus burden in cases with STEMI (1). In one more study, Sönmez et al. showed high levels of SCUBE1 both in the STEMI and non-STEMI patients (2). On the other hand, Özkan et al. found that SCUBE-1 was not a useful marker for unstable angina pectoris and acute coronary syndrome. The results of Özkan et al. suggested that further studies are necessary to show the association between SCUBE-1 and acute

coronary syndrome (3). Yılmaz et al. investigated the relationship between return of spontaneous circulation (ROSC) in cases with cardio-pulmonary resuscitation and serum SCUBE-1 levels and showed SCUBE-1 was higher in the ROSC group compared with the mortality cases (4). One of the important causes of mortality in COVID-19 is thromboembolic pathogenesis (5). Toprak et al. presented SCUBE1 as one of the main contributing factors of thrombotic complications, which is an increased cause of morbidity and mortality in COVID-19, according to the results of their study (6). Dirican et al. found high SCUBE-1 in cases with pulmonary embolism, and they recommended SCUBE-1 as a new diagnostic biomarker with high sensitivity (7). In an empirical study, Aköz et al. showed that SCUBE-1 is an early predictor of acute mesenteric ischemia and might be useful in detecting irreversible intestinal damage (8). In different experimental research, Türkmen et al. found that SCUBE-1 could use as an early predictor of acute ischemic stroke according to SCUBE-1 from the first hour of the persuaded stroke and continued elevated until the sixth hour verified (9).

In conclusion, in light of the mentioned literature, SCUBE-1 can be used as a predictor of thromboembolic events.

Keywords: SCUBE-1, thromboembolic events, myocardial infarction

Conflict of interest

The authors declared no conflict of interest.

Funding

No funding was used for the study.

Acknowledgments

None to declare.

Authors' contributions

Concept: H.Ş.A., Design: H.Ş.A., Data Collection or Processing: H.Ş.A., Analysis or Interpretation: H.Ş.A., Literature Search: H.Ş.A., Writing: H.Ş.A.

References

1. Yıldırım A, Küçükosmanoglu M, Koyunsever NY, Cekici Y, Dogdus M, Saracoglu E, et al. Association between serum SCUBE1 levels and thrombus burden in patients with ST-segment elevation myocardial infarction. *Acta Cardiol.* 2021 Sep;76(7):777-784. doi: 10.1080/00015385.2020.1852753.
2. Sonmez E, Turkdogan KA, Karabacak M, Civelek C, Yilmaz C, Ozer OF, et al. The diagnostic role of signal peptide-C1r/C1s, Uegf, and Bmp1-epidermal growth factor domain-containing protein 1 in non-ST-elevation acute coronary syndrome. *Am J Emerg Med.* 2015 Jan;33(1):21-4. doi: 10.1016/j.ajem.2014.09.047.
3. Özkan A, Sönmez E, Özdemir S, Özer F, Muharrem N, Gülen B, et al. The Diagnostic Value of SCUBE1 in Unstable Angina Pectoris Patients. *Eurasian J Emerg Med.* 2016;15:167-171. doi: 10.5152/eajem.2016.83997.
4. Yılmaz C, Gülen B, Sönmez E, Akbay D, Söğüt Ö, Özdemir S, et al. Serum SCUBE-1 Levels and Return of Spontaneous Circulation Following Cardiopulmonary Resuscitation in Adult Patients. *Avicenna J Med.* 2022 Sep 5;12(3):148-153. doi: 10.1055/s-0042-1755389.
5. Algın A, Özdemir S. Evaluation of the predictability of platelet mass index for short-term mortality in patients with COVID 19: A retrospective cohort study. *J Contemp Med* 2021;11(5):728-33. doi:10.16899/jcm.973825.
6. Toprak K, Kaplangoray M, Palice A, Taşcanov MB, İnanır M, Memioğlu T, et al. SCUBE1 is associated with thrombotic complications, disease severity, and in-hospital mortality in COVID-19 patients. *Thromb Res.* 2022 Dec;220:100-6. doi: 10.1016/j.thromres.2022.10.016.
7. Dirican N, Duman A, Sağlam G, Arslan A, Ozturk O, Atalay S, et al. The diagnostic significance of signal peptide-complement C1r/C1s, Uegf, and Bmp1-epidermal growth factor domain-containing protein-1 levels in pulmonary embolism. *Ann Thorac Med.* 2016 Oct-Dec;11(4):277-282. doi: 10.4103/1817-1737.191876.
8. Aköz A, Türkdöğün KA, Kahraman Çetin N, Kum S, Duman A, Türe M, et al. Predicting critical duration and reversibility of damage in acute mesenteric ischemia: An experimental study. *Ulus Travma Acil Cerrahi Derg.* 2018 Nov;24(6):507-513. doi: 10.5505/tjtes.2018.69710.
9. Turkmen S, Mentese S, Mentese A, Uzun Sumer A, Saglam K, Yulug E, et al. The value of signal peptide-CUB-EGF domain-containing protein 1 and oxidative stress parameters in the diagnosis of acute mesenteric ischemia. *Acad Emerg Med.* 2013 Mar;20(3):257-64. doi: 10.1111/acem.12096.