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# D-Dimer as a Prognostic Factor in a Tertiary Center Intensive Coronary Care Unit

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## Abstract

**Introduction:** D-dimer is a small protein fragment produced during fibrinolysis. High D-dimer levels were shown to have prognostic impact in critically ill patients. Nevertheless, data regarding D-dimer's prognostic impact among tertiary care intensive coronary care unit (ICCU) patients is scarce.

**Material and method:** All patients admitted to the ICCU between 1-12/2020 were prospectively included. Based on admission D-dimer level, patients were categorized into low and high D-dimer groups (< 500 ng/ml and ≥ 500 ng/ml) and also to age-adjusted D-dimer cutoff (500 ng/ml for ages ≤ 50 years old and age*10 for ages>50 years old).

**Results and discussion:** A total of 959 consecutive patients were included, including 296 (27.4%) and 663 (61.3%) patients with low and high D-Dimer levels, respectively. Patients with high D-dimer level were older compared with patients with low D-dimer level (age 70.4 ± 15 and 59 ± 13 years, p = 0.004) and had more comorbidities. The most common primary diagnosis on admission among the low D-dimer group was acute coronary syndrome (ACS) (74.3%), while in the high D-dimer group it was a combination of ACS (33.6%), cardiac structural interventions (26.7%) and various arrhythmias (21.1%). High D-dimer levels were associated with increased mortality rate, even after adjustment for age, gender, comorbidities and left ventricular ejection fraction (LVEF). High D-dimer levels were independently associated with increased overall 1-year mortality rate (HR = 5.8; 95% CI; 1.7-19.1; p = 0.004).

**Conclusion:** Elevated D-dimer levels on admission in ICCU patients is an independently poor prognostic factor for in-hospital morbidity and 1-year overall mortality rate following hospitalization.

## Keywords

dimer, intensive coronary care unit, critical ill patients

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## Introduction

D-dimer is a plasmin-derived soluble degradation product of cross-linked fibrin resulting from ordered breakdown of thrombi by the fibrinolytic system.[1,2] D-dimer was initially found to be a valuable marker for coagulation and fibrinolytic system activation, linked with various venous and arterial thrombotic events, as well as disseminated intravascular coagulation (DIC).[1,3] It was also shown to be an important prognostic

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factor in multiple diseases including various malignancies,[1,4–6] sepsis,[7,8] aortic dissection,[9,10] acute stroke,[11,12] and recently among COVID-19 patients.[13–15] Although robust data exists showing D-dimer to be a strong predictor for overall mortality among critically ill patients,[16–21] and although recent studies suggest a prognostic role among stable coronary patients[22,23] as well as among acute coronary syndrome (ACS) patients or after percutaneous coronary procedures,[24–26] data regarding its prognostic role among contemporary tertiary care intensive coronary care unit (ICCU) patients are scarce.[18] Notably, although both general ICU and ICCU patients are critically ill patients, the dominating illness is in these two medical settings is significantly different. In contrast to trauma, post major abdominal surgeries, and sepsis with multi-organ failure which are dominant in general ICU setting, the dominant illness among ICCU patients is cardiac failure of various etiologies (large infarct, previous cardiomyopathy, major valvular dysfunction) with preserved function of most extra-cardiac organs except of the very extreme cases. Furthermore, while many general ICU patients undergo major surgical procedures which have major systemic impacts including inflammatory and coagulation ones,[27] most ICCU patients undergo selective trans-cutaneous intra-vascular catheterization procedures (weather coronary or valvular) which do not impose the same systemic changes.. Hence, the aim of our study was to evaluate D-dimer levels impact on 1-year mortality rate among tertiary center ICCU patients, as well as to characterize the baseline features, medical background and admission profile of patients with low versus high D-dimer levels and to evaluate D-dimer's association with in-hospital interventions and complications.

## Methods

All patients admitted to the ICCU at Sha'are Zedek Medical Center between 1-12/2020 were prospectively included. Based on routine D-dimer level on admission, patients were categorized into low and high D-dimer groups (< 500 ng/ml and ≥ 500 ng/ml).[1] D-dimer level in all patients was determined via automated latex enhanced immunoassay (Hemosil, MA, USA). Since the normal range of D-dimer levels increase significantly with age,[1] we described the rate of increased D-dimer based on patients' age-groups. Demographic data, presenting symptoms, comorbid conditions, medications and physical examination were systematically recorded. Laboratory and imaging data were collected as well. Given age-adjusted D-dimer cutoff (being 500 ng/ml for ages ≤ 50 years old and age*10 for ages>50 years old) which has become consensus in the field of venous thromboembolic disease[1,28] we confirmed our study results by analysis of age-adjusted D-dimer cutoff as well.

In our study, ACS included both STEMI and NSTEMI patients. We use the term "cardiac structural interventions" to refer to all percutaneous interventions aimed to treat cardiac structural disease including valvular disease (Trans-cutaneous aortic valve replacement, mitral valve clip, etc), atrial septal defect (ASD)/ ventricular septal defect VSD closure, closure of left atrial appendage, and others.

As the vast majority of data on diagnostic and prognostic yield of D-dimer to date relates to thromboembolic disease and given the fact that age-adjusted D-dimer cutoff (being 500 ng/ml for ages ≤ 50 years old and age*10 for ages>50 years old) has become consensus in the field of venous thromboembolic disease[1,28,29] we confirmed our study results by analysis of age-adjusted D-dimer cutoff as well.

The Institutional review board approved the study on the basis of strict maintenance of participants' anonymity by de-identifying during database analysis. No individual consent was obtained. Moreover, the authors have no conflicts of interest to declare. No Funding was applied for the study. All methods were performed in accordance with the relevant guidelines and regulations.

### Study Outcomes

The primary outcome of our study was overall mortality, assessed at 1-year from time of index hospitalization. Overall mortality rate was determined from the Israeli Ministry of Internal Affairs. The study secondary outcomes included: a) comparison of patients' characteristics among the low and high D-dimer groups; b) in-hospital interventions and complications during the index hospitalization among both groups.

### Statistics

Characteristics were described as numbers and percentages for categorical variables and by means ± standard deviations or median with interquartile ranges for continuous variables. Relations between categorical variables were evaluated by chi-square and Fisher's exact tests. The effect of categorical variables on continuous measurements was tested by student-T and Mann-Whitney tests. The choice of a parametric or nonparametric test depended on the distribution of a continuous variable. Mortality was analyzed by applying stepwise backward Cox proportional hazards model adjusted for D-dimer groups (using <500 ng/ml as reference group), age, gender, prior cardiac intervention, various cardiac risk factors (all factors appearing in Table 1) and EF<40. All tests were two-sided. $P < 0.05$ was considered statistically significant. Analyses were carried out using SPSS Statistics for Windows, Version 25.0. (IBM Corp, Armonk, NY, USA).

## Results

A total of 1082 consecutive patients were admitted during 2020, of them 959 (89%) patients had D-dimer levels on admission and comprised the study population. Two hundred and ninety-six (27.4%) patients and 663 (61.3%) patients had low <500 ng/ml and high ≥500 ng/ml D-dimer levels, respectively.

### Study Population

Mean age was 67 ± 16 years old, and 70% were males. The incidence of high D-dimer levels varied among different age groups (Figure 1). While only minority of patients aged 40-60 years old

**Table 1.** Baseline Characteristics & Background Illness Among low & High D-dimer Groups.

| | D-Dimer level | | | |
|---|---|---|---|---|
| Clinical diagnosis | <500 (n = 296) | > = 500 (n = 663) | Total (n = 959) | p-value |
| **Baseline characteristics & Background illness** | | | | |
| Age | 58.9 ± 13 | 70.4 ± 15.3 | 67 ± 16 | <0.0001 |
| Males | 208 (84) | 466 (64) | 674 (70.3) | <0.0001 |
| BMI | 28.2 ± 4.9 | 27.4 ± 5.7 | 27.7 ± 5.5 | 0.005 |
| Hypertension, n (%) | 143 (48.3) | 441 (66.5) | 584 (60.9) | <0.0001 |
| Hyperlipidemia, n (%) | 145 (49.0) | 344 (52.0) | 489 (51.0) | 0.394 |
| Diabetes Mellitus, n (%) | 95 (32.1) | 248 (37.4) | 343 (35.8) | 0.113 |
| Smoking, n (%) | 135 (45.6) | 149 (22.5) | 284 (29.6) | <0.0001 |
| IHD | 85 (28.7) | 186 (28.1) | 271 (28.3) | 0.87 |
| s/p CABG | 7 (2.4) | 43 (6.5) | 50 (5.2) | 0.007 |
| CHF | 16 (5.4) | 126 (19) | 142 (14.8) | <0.0001 |
| LVEF <40% | 59 (19.9) | 183 (27.6) | 242 (25.2) | 0.012 |
| ICD | 2 (0.9) | 41 (6.2) | 43 (4.5) | 0.001 |
| Atrial Fibrillation, n (%) | 21 (7.1) | 112 (16.9) | 133 (13.9) | <0.0001 |
| PAD | 10 (3.4) | 46 (6.9) | 56 (5.8) | 0.035 |
| COPD, n (%) | 5 (1.7) | 71 (10.7) | 76 (7.9) | <0.0001 |
| Pulmonary Hypertension, n (%) | 0 (0) | 51 (7.1) | 51 (5.3) | <0.0001 |
| Renal failure, n (%) | 14 (4.7) | 145 (21.9) | 159 (16.6) | <0.0001 |
| Dialysis | 2 (0.7) | 20 (3) | 22 (2.3) | 0.033 |
| Any Malignancy, n (%) | 11 (3.7) | 81 (12.2) | 92 (9.6) | <0.0001 |
| Anemia, n (%) | 5 (1.7) | 47 (7.1) | 52 (5.4) | <0.0001 |
| Post-COVID-19, n (%) | 0 (0) | 11 (1.7) | 11 (1.1) | 0.026 |
| s/p CVA | 13 (4.4) | 60 (9) | 73 (7.6) | 0.012 |
| Debilitated | 1 (0.3) | 21 (3.2) | 22 (2.3) | 0.004 |

BMI – Body mass index; IHD – Ischemic heart disease; CABG – Coronary artery bypass graft; CHF – Congestive heart failure; LVEF – Left ventricular ejection fraction; ICD - Implantable Cardioverter Defibrillator; PAD – Peripheral arterial disease; COPD – Chronic obstructive pulmonary artery disease; CVA – Cerebrovascular accident.

had high D-Dimer levels, the majority at ages <40 and >60 years old had high D-dimer levels, with an increasing D-dimer levels at advanced age. Patients' characteristics and co-morbidities among the low and high D-dimer groups is shown in Table 1. The high D-dimer group was characterized by older patients (70.4 ± 15.3 vs 58.9 ± 13, years old; p = 0.0001), more females gender (36% vs 16%; p 0.0001), with significantly increased co-morbidities including hypertension (HTN), atrial fibrillation (AF), congestive heart failure (CHF), peripheral arterial disease (PAD), cerebrovascular accident, chronic obstructive pulmonary disease, renal dysfunction as well as dialysis, pulmonary hypertension, malignancy and anemia.

## *Diagnosis on Admission*

The primary diagnosis on admission is presented in Table 2. The main diagnosis in the low D-Dimer group was ACS 220/296 (74.4%) as compared with only 223/663 (33.6%) in the high D-dimer group (p = 0.0001). On the other hand, cardiac arrhythmias were more common among high D-dimer group (21.1% vs 8.8%; p = 0.0001) as were structural interventions (26.7% vs 4.4%; p 0.0001); CHF exacerbation, sudden cardiac death resuscitation, sepsis, tamponade (in the context of an urgent procedure or as de novo diagnosis), pulmonary emboli and shock.

## *Mortality and Complications Rate*

The high D-dimer group had more complications during their hospitalization period as compared with the low D-dimer group (20.4% vs 6.1%, P < 0.0001). These included more cases of CHF exacerbation, shock, renal failure, bleeding and blood transfusion, stroke, and sepsis (Table 3).

In-hospital mortality rate was higher in the high D-dimer group [40/663 (6%) versus 0/296; p < 0.0001]. Moreover, the 1-year overall mortality rate was higher in the high D-dimer group as compared with the low D-dimer group [80/663 (12.1%) versus 3/296 (1%); p < 0.0001]. (Figure 2).

After a multivariate analysis for overall mortality, D-dimer level was found to be independently associated with 1-year mortality rate [HR 5.76 [1.74, 19.1], p = 0.004] and was the strongest risk factor for mortality even compared with age, CHF, PAD, renal failure, AFL, and LVEF which were all independently associated with higher mortality rate (Table 4).

## *Mortality According to ICCU Admission Diagnosis*

The main diagnoses upon ICCU admissions were ACS (n = 443); structural percutaneous interventions (n = 190); arrhythmias (n = 166); and CHF exacerbation (n = 108). Apart from ACS in which there were significantly less patients with high D-dimer levels compared with low D-dimer levels, in all

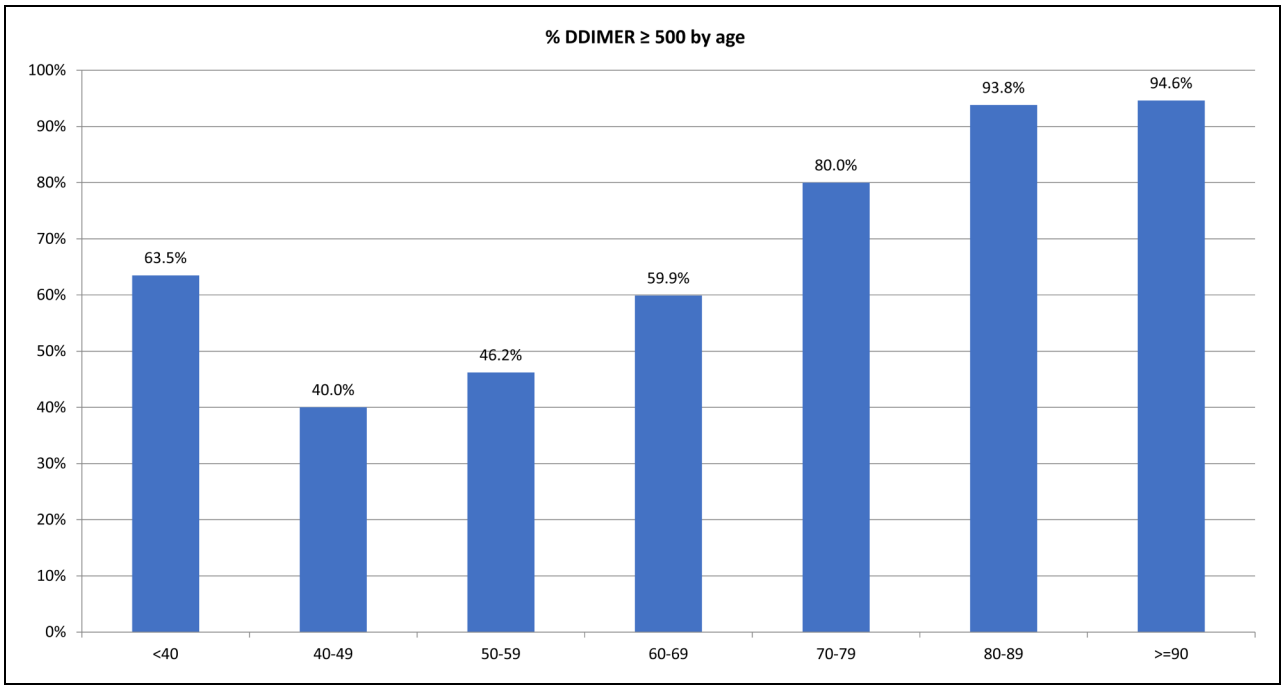


**Figure 1.** Incidence of high D-dimer levels among ICCU patients according to age distribution.

other diagnoses there were more patients with high D-dimer levels as seen in Table 2. The Kaplan Meier survival analysis according to low and high D-dimer levels in each of these diagnoses subgroups (Figure 3) were not significant apart for ACS subgroup, where high D-dimer levels were associated with significantly increased mortality ($p < 0.001$).

### *Age-Adjusted D-Dimer Analysis*

There were 396 (41%) and 563 (59%) patients with low and high age-adjusted D-dimer levels, respectively. The incidence of high age-adjusted D-dimer level according to patients' age groups (supp Fig 1) was similar to the absolute high D-dimer incidence, revealing majority of patients of age <40 or >60 years old with high age-adjusted D-dimer level. As expected from the use of age-adjusted D-dimer levels, the percent of age-adjusted high D-dimer level among the elderly was less than that of the absolute high D-dimer level.

Age-adjusted high D-dimer admission level was significantly associated with an increased overall 1-year mortality rate [69/563 (12.3%) versus 14/396 (3.5%); $p < 0.001$]. This was confirmed via KM survival analysis (supp Fig 2) and by multivariate analysis for overall mortality (Table 5), revealing high age-adjusted D-dimer level to be an independent predictor of increased 1-year overall mortality rate [HR 2.5; [1.3, 4.81], $p = 0.006$].

## Discussion

In this large prospective trial in a tertiary care ICCU, high D-dimer levels were correlate with older age, more co-morbidities, more complications during hospitalization and higher in-hospital and 1-year mortality rate. Even after multivariate analysis for confounders, high D-dimer levels were related to worse prognosis. Most importantly, high D-dimer level was the strongest predictor for mortality with a HR of 5.76.

Similar with most prior publications, older patients had an increased percent of elevated D-dimer levels.[1,13,16,28,29] Nevertheless, we have also noticed an increased percent of younger (<40 y/o) patients with elevated D-dimer levels. To explore the explanation for this finding we compared the various admission diagnoses between young <40 y/o) and older ICCU patients and found a significantly increased incidence of myocarditis, pulmonary emboli, and CHF among the young patients (43% vs 16%, p 0.02). Thereafter, we found these diagnoses were all significantly associated with increased D-dimer levels ($p = 0.01$). Thus, we attribute the increased percent of elevated D-dimer among young ICCU patients to increased incidence of myocarditis, pulmonary emboli and CHF. Notably, the CHF in the young ICCU patients included early-onset DCM, severe myocarditis cases with LV dysfunction, and patients with extensive MI leading to significantly reduced LF function.

Prior studies have shown an elevated D-dimer levels among elderly patients[1,18,30] and in many co-morbidities including renal failure,[1,18] cancer,[1,4–6] and sepsis.[1,7,8] Recently, D-dimer was shown to be an important prognostic factor among COVID-19 patients.[13–15] Nevertheless, our study emphasizes the fact that high D-dimer level correlates with mortality in ICCU patients, independently of their reason for admission. Notably, analysis of high D-dimer level impact on 1-year mortality rate among subgroups with different ICCU admission

**Table 2.** Primary Diagnosis Leading to Intensive Coronary Care Unit (ICCU) Admission Among Low& High D-dimer Groups.

| Clinical diagnosis | D-Dimer level <500 (n = 296) | D-Dimer level >= 500 (n = 663) | Total (n = 959) | p-value |
|---|---|---|---|---|
| ACS - STEMI, n (%) | 97 (32.8) | 130 (19.6) | 227 (23.7) | <0.0001 |
| ACS- NSTEMI, n (%) | 123 (41.6) | 93 (14.0) | 216 (22.5) | <0.0001 |
| CHF, n (%) | 9 (3.0) | 99 (14.9) | 108 (11.3) | <0.0001 |
| Sudden Cardiac Death | 0 | 12 (1.8) | 12 (1.2) | 0.02 |
| Any Rhythm disturbance, n (%) | 26 (8.8) | 140 (21.1) | 166 (17.3) | <0.0001 |
| Any Tachycardia, n (%) | 12 (4.1) | 63 (9.5) | 75 (7.8) | 0.004 |
| VT (non-sustained, sustained)/VF | 7 (2.3) | 42 (6.3) | 49 (5.1) | 0.01 |
| AF/AFL | 4 (1.3) | 22 (3.3) | 26 (2.7) | 0.08 |
| Any Bradycardia, n (%) | 12 (4.1) | 62 (9.4) | 74 (7.7) | 0.005 |
| Pulmonary Emboli | 2 (0.7) | 43 (6.5) | 45 (4.7) | < 0.0001 |
| Myocarditis, n (%) | 13 (4.4) | 13 (2.0) | 26 (2.7) | 0.05 |
| Tamponade, n (%) | 0 (0) | 13 (2.0) | 13 (1.4) | 0.013 |
| Any shock, n (%) | 7 (2.4) | 67 (10.1) | 74 (7.7) | <0.0001 |
| Sepsis, n (%) | 0 (0) | 29 (4.4) | 29 (3.0) | <0.0001 |
| Percutaneous coronary interventions, n (%) | 13 (4.4) | 177 (26.7) | 190 (19.8) | <0.0001 |
| TAVI, n (%) | 2 (0.7) | 120 (18.1) | 122 (12.7) | <0.0001 |
| Mitral clip | 1 (0.3) | 9 (1.4) | 10 (1) | 0.135 |

ACS – Acute Coronary Syndrome; STEMI – ST segment myocardial infarction; NSTEMI – Non ST segment myocardial infarction; CHF – Congestive heart failure; VT – Ventricular tachycardia; VF – Ventricular fibrillation; AF – Atrial fibrillation; AFL – Atrial flutter; TAVI – Trans catheter aortic valve implantation.

**Table 3.** In-Hospital Complications Among Low & High D-dimer Groups.

| In Hospital complications | D-Dimer level <500 (n = 296) | D-Dimer level >= 500 (n = 663) | Total (n = 959) | p-value |
|---|---|---|---|---|
| CHF | 4 (1.4) | 26 (3.9) | 30 (3.1) | 0.022 |
| Shock | 3 (1) | 37 (5.6) | 40 (4.2) | 0.001 |
| MI | 1 (0.3) | 6 (0.9) | 7 (0.7) | 0.34 |
| Ventricular arrhythmia | 4 (1.4) | 17 (2.6) | 21 (2.2) | 0.3 |
| Renal failure | 0 (0) | 49 (7.4) | 49 (5.1) | < 0.0001 |
| Bleeding | 4 (1.4) | 50 (7.5) | 54 (5.6) | < 0.0001 |
| CVA/ | 0 (0) | 7 (1.1) | 7 (0.7) | 0.076 |
| Sepsis | 1 (0.3) | 13 (2) | 14 (1.5) | 0.05 |
| Total complications | 18 (6.1) | 135 (20.4) | 153 (16) | < 0.0001 |

CHF – Congestive heart failure; MI – Myocardial infarction; CVA – Cerebrovascular accident.

diagnoses, showed a trend for increased mortality among all main diagnoses, although reaching significance only among ACS subgroup., which was the largest subgroup. We attribute the non- significant result among other subgroups to the relatively small number of patients in these subgroups and to the fact that the patients among these subgroups are very much skewed to the elevated D-dimer group (for example 99/108 CHF patients had elevated D-dimer; Table 2) .

The prognostic impact of D-dimer among general (non-cardiac) intensive care (ICU) patients, confirmed via multiple studies,[16–21,31] was rarely addressed among ICCU patients.[18] Spring et al[18] evaluated 144 patients admitted to cardiothoracic ICU who had D-dimer level taken upon admission, revealing a significant correlation between D-dimer level and renal dysfunction but no significant association between D-dimer level and in-hospital mortality. Similar result showing no association of D-dimer with ICU patients' in-hospital mortality was published by Shitrit et al.[31] Notably, both studies[18,31] included medical and surgical ICU patients and the negative association between D-dimer and mortality was attributed to inclusion of surgical cases, in whom elevated D-dimer levels could result from the surgical procedure itself.[1,18,31–33] The strong significant association between D-dimer levels and 1-year mortality rate revealed in our study may be explained by absence of surgical patients, large number of patients (almost 1000 patients) and by the relatively long-term follow-up. Moreover, prior studies, involving non-surgical ICU patients, have also shown the correlation between high D-dimer levels and an increased in-hospital mortality rate, as shown in our study.[16,21]

The primary diagnosis leading to ICCU admission among patients with high and low D-dimer levels differed significantly. In contrast with the dominant ACS among the low D-dimer group (74.4%), the high D-dimer group patients were admitted due to combination of ACS, valvular interventions, cardiac arrhythmias and shock. Notably, a relative minority of the high D-dimer group (33.6%) were admitted due to ACS. This does not suggest by any means that coronary disease (stable or unstable) is not associated with elevated D-dimer levels, as this was firmly established by multiple large studies.[22–24,28] We attribute the relatively low D-dimer level among many of the ACS patients to their relatively young age and their healthier general status, without significant other comorbidities. This is characteristic of many ICCU patients whose primary diagnosis, leading to ICCU hospitalization, is ACS. These patients are many times hemodynamically stable, and the reason for ICCU admission is the need for intensive ECG monitoring

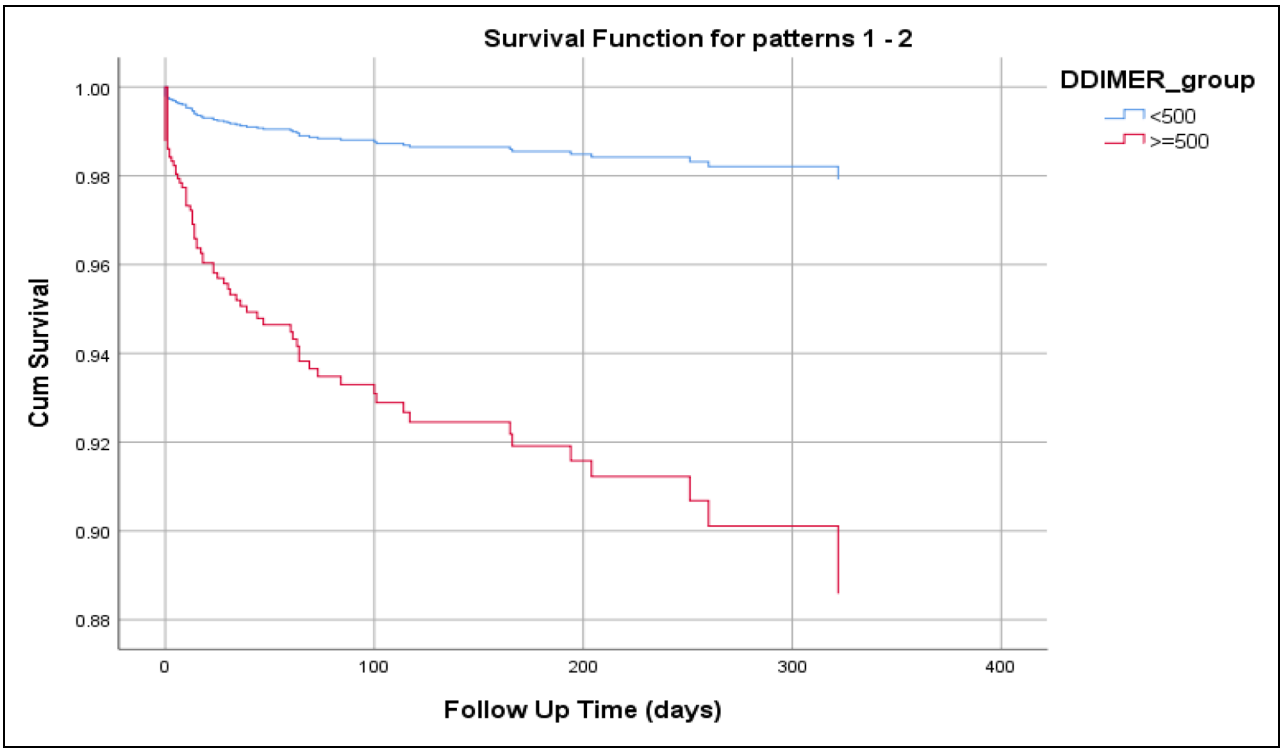


**Figure 2.** Kaplan Meier Cumulative survival analysis according to ICCU admission D-dimer level.

**Table 4.** Parameters Associated with Increased or Reduced Mortality on Multivariate Cox Regression Analysis.

| | B | SE | Wald | Sig. | Exp(B) | 95.0% CI for Exp(B): lower | 95.0% CI for Exp(B): Upper |
|---|---|---|---|---|---|---|---|
| DDIMER_group | 1.752 | .611 | 8.216 | .004 | 5.766 | 1.740 | 19.104 |
| Age | .045 | .011 | 15.774 | .000 | 1.046 | 1.023 | 1.070 |
| Acute coronary syndrome | −1.070 | .356 | 9.034 | .003 | .343 | .171 | .689 |
| Congestive heart failure | .616 | .283 | 4.727 | .030 | 1.852 | 1.063 | 3.228 |
| Cardiac intervention | −1.609 | .388 | 17.237 | .000 | .200 | .094 | .428 |
| Peripheral arterial disease | .843 | .393 | 4.601 | .032 | 2.324 | 1.075 | 5.024 |
| Pulmonary Hypertension | −1.011 | .447 | 5.117 | .024 | .364 | .152 | .874 |
| Renal Failure | .802 | .265 | 9.124 | .003 | 2.230 | 1.325 | 3.752 |
| Atrial fibrillation | .560 | .284 | 3.900 | .048 | 1.751 | 1.004 | 3.054 |
| LVEF < 40% | .825 | .263 | 9.847 | .002 | 2.282 | 1.363 | 3.821 |

due to the fear of ACS-related ventricular malignant arrhythmias. Otherwise, many of these patients have no other comorbidities and their cardiac function might be preserved without CHF manifestations.

During the last decade the use of age-adjusted D-dimer cutoff has gained popularity and became almost a consensus in the diagnostic algorithm of venous thromboembolic disease.[1,34] Nevertheless, most prior studies regarding the use of D-dimer in critically ill patients as well as ACS patients still use a constant cutoff, which is mostly 500 ng/ml.[18,20,21,23–25] Thus, in our study we used a D-dimer cutoff value of 500 ng/ml. Nevertheless, to accommodate for the increasing use of age-adjusted cutoff we confirmed our main results by age-adjusted D-dimer levels as well. Hence, revealing similar percent of elevated d-dimer levels at ages < 40 and > 60 years old, with significantly increased mortality for ICCU patients with high age-adjusted D-dimer levels.

Based on our study results revealing both in-hospital and 1-year post discharge increased mortality among ICCU patients with elevated D-dimer levels, we recommend increasing the monitoring level of these ICCU patients during their admission, as well as rigorous and frequent post-discharge clinical follow-ups, to ensure early diagnosis of developing medical issues and targeted efforts for their early resolution. Importantly, as of today there are numerous models predicting general ICU mortality including APACHE, SAPS II, and othes[29] but few if any such models for ICCU patients.[35] Accordingly, the result of the current study might held develop a contemporary mortality model for ICCU patients as well.

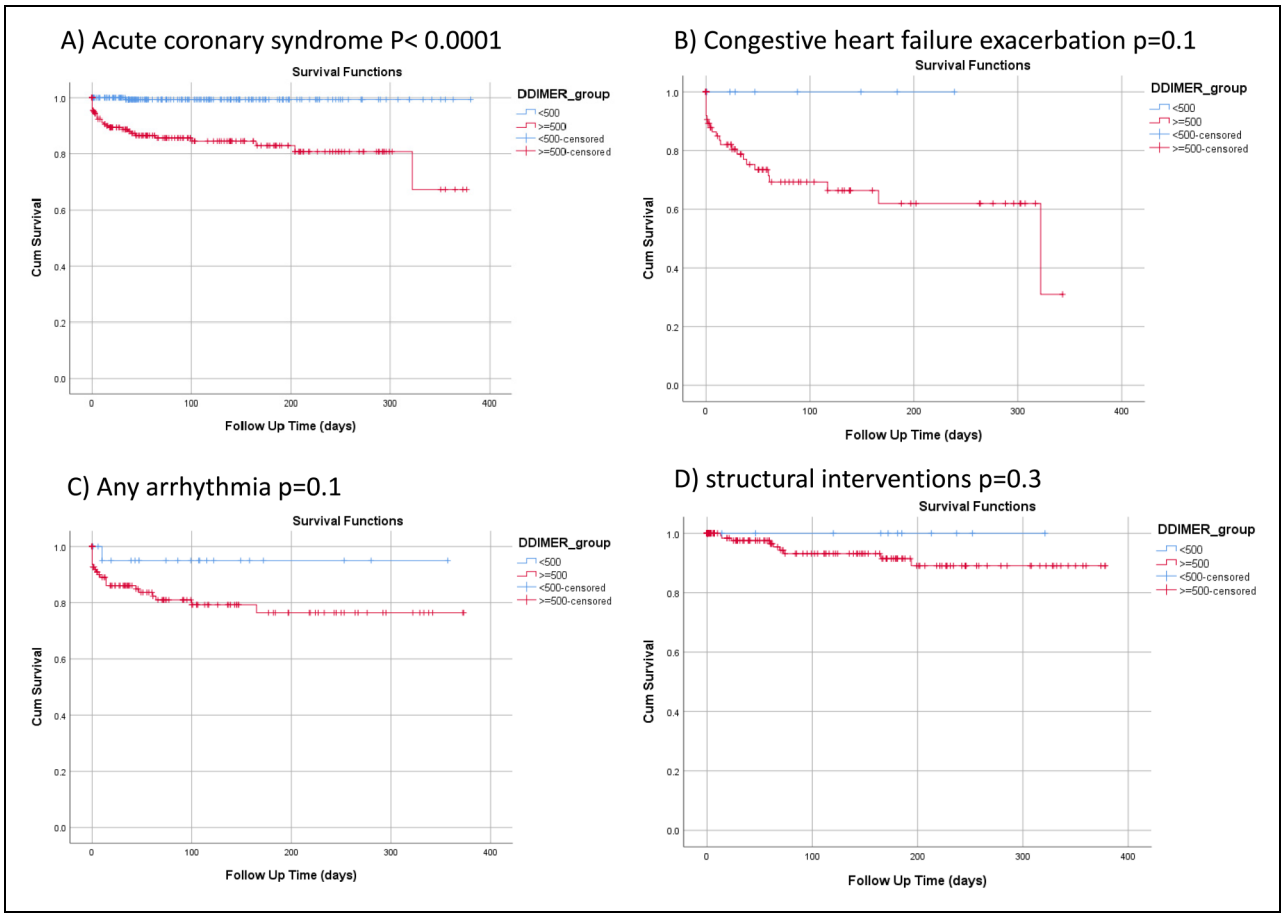


**Figure 3.** Kaplan Meier Cumulative survival curves according to ICCU admission D-dimer level in subgroups with different admission diagnosis

**Table 5.** Parameters Associated with Increased or Reduced Mortality on Multivariate Cox Regression Analysis, Using Age-Adjusted D-dimer Level.

| | B | SE | Wald | Sig. | Exp(B) | 95.0% CI for Exp(B): lower | 95.0% CI for Exp(B): Upper |
|---|---|---|---|---|---|---|---|
| Age-adjusted DDIMER_group | 0.920 | .332 | 7.660 | .006 | 2.5 | 1.300 | 4.81 |
| Age | .060 | .012 | 25.346 | .000 | 1.06 | 1.037 | 1.086 |
| Gender | .469 | .283 | 2.746 | 0.1 | 0.62 | .360 | 1.089 |
| Acute coronary syndrome | 1.138 | .357 | 10.170 | .001 | 0.32 | .159 | 0.645 |
| Congestive heart failure | .628 | .288 | 4.745 | .03 | 1.87 | 1.065 | 3.29 |
| Cardiac intervention | −1.660 | .389 | 18.244 | .000 | 0.19 | .09 | 0.3 |
| Diabetes Mellitus | .450 | .253 | 3.162 | 0.075 | 1.56 | .955 | 2.57 |
| Peripheral arterial disease | .933 | .398 | 5.501 | .02 | 2.54 | 1.166 | 5.54 |
| Pulmonary Hypertension | −1.077 | .452 | 5.689 | .02 | 0.34 | .140 | 0.82 |
| Renal Failure | .725 | .269 | 7.255 | .007 | 2.06 | 1.218 | 3.5 |
| Atrial fibrillation | .604 | .285 | 4.484 | .034 | 1.83 | 1.046 | 3.2 |
| LVEF < 40% | .775 | .273 | 8.095 | .004 | 2.17 | 1.273 | 3.7 |

## *Limitations*

The study has several limitations, including: 1) a single center study, although based on a large tertiary Israeli center with almost 1000 ICCU admission per year; 2) absence of baseline D-dimer level prior to ICCU admission. Notably though, we do not aim to prove that elevated D-dimer levels were result of their admission but rather to suggest that simple clinical testing of D-dimer on admission is a strong predictor for mortality among these patients.

## *Summary*

The current trial which included almost 1000 consecutive patients admitted to tertiary center ICCU, demonstrated that

High D-dimer level was independently associated with increased 1-year mortality rate even after adjustment to age and various comorbidities. Moreover, high D-dimer level was the strongest single predictor for mortality with a HR >5. Further studies are needed to better understand this phenomenon.

## Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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## Ethical Approval

Ethical approval to report this case was obtained from Shaare Zedek INSTITUTIONAL REVIEW BOARD (SZMC-0431-20).

## Informed Consent

Informed consent for patient information to be published in this article was not obtained because the data was obtained from patients' charts.

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## Supplemental Material

Supplemental material for this article is available online.

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