Real-world data on the effect of anticoagulants to prevent or treat DIC

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Abstract

Disseminated intravascular coagulation (DIC) is a pathological process characterized by a systemic activation of the blood coagulation system, leading to subsequently clot formation, blood vessel obstruction and organ dysfunction. The large consumption of platelets and coagulation factors in this process may in turn cause bleeding, which further worsens the patient's condition and decreases the chances of survival [1]. DIC is usually secondary to an underlying condition such as systemic inflammatory response syndrome (SIRS), sepsis, trauma, malignancy, heat stroke or hyperthermia. Between 30% and 50% of sepsis patients develop DIC. Sepsis severity positively correlates with DIC incidence and therefore mortality [2]. DIC incidence ranges between 7% (mild sepsis) and 73% (septic shock) [3] and DIC mortality ranges between 10% and 50%. We investigated the influence of anticoagulants when provided to patients after the diagnosis of sepsis, both on the development of DIC and outcome.

We selected 89,694 SIRS/sepsis patients from the Philips eICU Research Institute database (ICD9 codes for SIRS/sepsis and SIRS/sepsis + organ failure). 3592 (4%) of these patients had a diagnosis of DIC during their ICU stay (ICD9 code or ISTH score >= 4). For the group of patients that received anticoagulants after a SIRS/sepsis +/- organ failure diagnosis we found a significant reduction (versus no anticoagulant treatment) in 1) the number of DIC diagnoses, 2) the mortality after DIC diagnosis and 3) the mortality without DIC diagnosis. For the group of patients that received anticoagulants after DIC diagnosis we found no benefit compared to no anticoagulant treatment.

Our results indicate that anticoagulant treatment may benefit septic patients in terms of DIC development and outcome.

Introduction

Disseminated intravascular coagulation (DIC) is a pathological process characterized by a systemic activation of the blood coagulation system, leading to subsequently clot formation, blood vessel obstruction and organ dysfunction. The large consumption of platelets and coagulation factors in this process may in turn cause bleeding, which further worsens the patient's condition and decreases the chances of survival [1]. DIC is usually secondary to an underlying condition such as systemic inflammatory response syndrome (SIRS), sepsis, trauma, malignancy, heat stroke or hyperthermia. Between 30% and 50% of sepsis patients develop DIC. Sepsis severity positively correlates with DIC incidence and therefore mortality [2]. DIC incidence ranges between 7% (mild sepsis) and 73% (septic shock) [3] and DIC mortality ranges between 10% and 50%. We investigated the influence of anticoagulants when provided to patients after the diagnosis of sepsis, both on the development of DIC and outcome.

Materials & Methods

We selected patients with a diagnosis of SIRS or sepsis from the Philips eICU Research Institute database (ICD9 codes 995.90, 995.91 and 995.93 for SIRS/sepsis and ICD9 codes 995.92, 995.94 for SIRS/sepsis + organ failure). We then used descriptive statistics to learn about the possible effects on anticoagulants (heparin or low molecular weight heparin) on the prevention or treatment of DIC. DIC was identified by the presence of the IC9 code 286.6 or the availability or possibility to calculate the ISTH DIC score. As measurements for fibrinogen and especially D-dimer/Fibrin Degradation Products were often lacking, we used a score of 4 instead of 5 as diagnostic for DIC.

Results

89,694 patients were documented with an ICD9 code related to the SIRS and/or sepsis. Of these, 27,894 patients had received anticoagulant treatment before the diagnosis of SIRS/sepsis and were excluded from further analysis. Of the remaining 61,800 patients, 2,779 (4.5%) developed DIC during their ICU stay, of which 1,184 (43%) died when hospitalized. Of the 59,021 patients who did not have an indication of DIC development, 7,059 (12%) died when hospitalized.

Mortality in the overall SIRS/sepsis population was 13%. Of the 41,738 SIRS/sepsis patients who did not receive any anticoagulant treatment, 6,214 (15%) died during their hospital stay. Of the 20,062 SIRS/sepsis patients who did receive anticoagulant treatment after this diagnosis, 2,029 (10%) died.

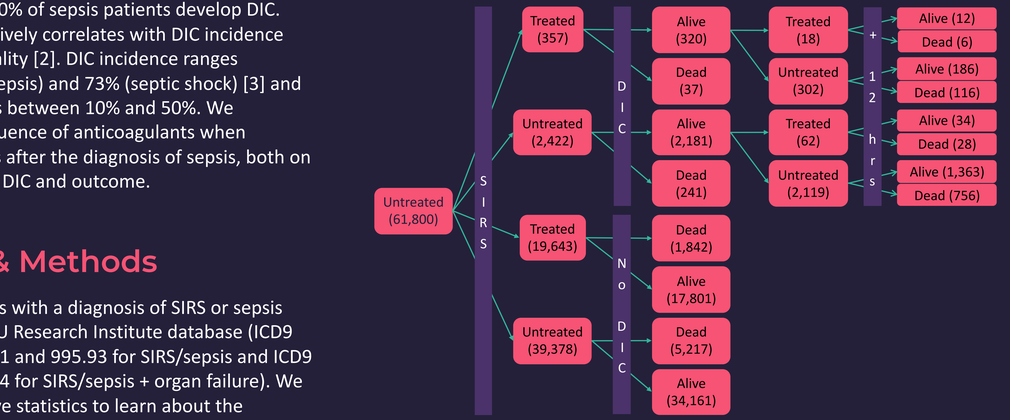

Figure 1: Data analysis flow diagram with a breakdown of the absolute patient numbers in each category

Anticoagulant treatment was defined as 'early' when it was provided before the diagnosis of DIC and as 'late' when it was provided within 12 hours after the diagnosis of DIC. Of the 41,800 patients who received no anticoagulant treatment after the diagnosis of SIR/sepsis, 2,422 (5.8%) developed DIC. The mortality in this group of DIC patients was 42%. Late anticoagulant treatment did not show an improvement in mortality (45%) for these patients. 357 patients (1.8%) developed DIC despite early treatment. The mortality in this early treated DIC population was also 45%.

Discussion

The development of SIRS/sepsis and subsequently DIC is associated with significant mortality (13% and 43% respectively in our study). Early treatment of SIRS/sepsis patients was associated with a reduced DIC development compared to no treatment (1.8% versus 5.8%). Moreover, anticoagulant treatment of SIRS/sepsis patients was associated with a lower mortality (10% versus 15% in the non-treated population). Anticoagulant treatment, either early or late, was not associated with a lower mortality in the subpopulation of patients who developed DIC (45%). Only the small DIC patient subgroup (18 patients) that received both early and late anticoagulant treatment showed a lower mortality (33%).

While the analysis of real-world data comes with several drawbacks (e.g. causal treatment effects can't be determined) and pitfalls (e.g. the under-reporting of diagnoses and the lack of sufficient diagnostics), the large availability of these data may point to interesting preliminary findings that warrant further (prospective or interventional) research studies.

Conclusion

Our results indicate that anticoagulant treatment may benefit septic patients in terms of DIC development and outcome. This effect seems to be strongly dependent on the timing and duration of the anticoagulant treatment. Further (prospective, interventional) research studies are needed to substantiate our early findings.

References

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