Coagulation parameters as predictors of DIC in patients with intact aortic aneurysm

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Summary
Clinically overt, preoperative, disseminated intravascular coagulation (DIC) is not common in patients with aortic aneurysm. However, cases with large and expanding aneurysm are especially prone for this coagulopathy. Contrary to the clinically overt form compensated DIC in patients with aortic aneurysm seems frequent and is probably underdiagnosed. The compensated DIC may be recognized, even without bleedings, by laboratory tests documenting the activated coagulation and fibrinolysis. We show that in about one third of patients with abdominal aorta aneurysm (AAA) compensated DIC can be identified. This enables the application of preoperative anticoagulation treatment to improve the intraoperative haemostasis.

Aneurysm morphology and activation of coagulation

The correlation between morphology of aneurysm and coagulation parameters is presented in the Table 1. According to Yamazumi et al. (31) and our data the diameter of abdominal aorta aneurysm is correlated with the preoperative activation of coagulation and fibrinolysis as seen by the markers prothrombin fragment F1+2, D-dimer, trombin-antithrombin complex (TAT), plasmin-antiplasmin complex (PIP). These data are compatible with the reports (1, 4, 6, 8, 10, 14, 15, 18, 19, 23, 26, 28, 29) that patients with a large diameter of the aneurysm (>7 cm) are especially at risk of coagulation abnormalities related to activated coagulation resulting from abnormal flow in the aneurysmatic sac.

Yamazumi and associates (31) also found a correlation between diameter and maximal thickness of intraluminal thrombus (r = 0.607; p = 0.0003) and an inverse correlation between strong tortuosity of the aorta, expressed as worst angle of abdominal aorta aneurysm (AAA), preoperative levels of D-dimer and TAT.

Since then many reports were published documenting the association between DIC and thoracoabdominal and abdominal aneurysms of different types:
- dissecting,
- ruptured, and
- intact.

Actually, large vascular aneurysm is listed among sepsis, malignancy, hepatic failure, trauma as one of the clinical conditions that may be associated with clinically overt DIC (22).

Aortic aneurysm and DIC

According to Müller-Berghaus three phases of disseminated intravascular coagulation can be differentiated. The continuous transition from phase I to phase II and III is typical for DIC (20, 21).
- In phase I only the presence of the underlying disease raises the suspicion of DIC. The presence of compensated
state of DIC may be recognized by laboratory evidence, even in absence of bleeding.

- In phase II bleedings from injuries, venous puncture sites, and functional impairment of organs (e.g., kidneys, lungs, liver) are observed. They are accompanied by decompensated activation easily recognized in coagulation tests.

- In phase III full-blown DIC occurs with accompanying multiorgan failure. This full-blown DIC is very resistant to correction and often fatal, since activation of coagulation is then widespread, progressive, and so massive that it exceeds the body's capability of replacing consumed factors and platelets (25). According to Mulcare et al. (19) incidence of full-blown DIC occurs during repair of ruptured aneurysm in at least 40% of patients.

Since the end of 1970 numerous case reports documenting an association between aortic aneurysm and consumption coagulopathy in patients with intact AA. Their results differ significantly as shown in Table 2. Comparison of data is very difficult. Different exclusion criteria were adopted by particular authors and aneurysm diameters of the patients vary. According to the frequently quoted results of Fisher et al., clinically overt DIC occurs preoperatively in 4% of patients with AA (8). But in his studied group DIC was documented only in patients with thoracoabdominal aortic aneurysm. In our group of AAA patients, only one (with aneurysm diameter 82 mm) had clinically overt DIC. Our results, like those of Fisher et al. seem to indicate that overt DIC occurs relatively seldom in AAA patients and only in case of large aortic aneurysm. This is confirmed by numerous case reports (1, 4, 6, 8, 10, 14, 15, 18, 19, 23, 26, 28, 29) which indicate that symptomatic DIC is mostly related to aortic aneurysm with diameter >7 cm and particularly to rapidly expanding aneurysms (2, 4, 12, 14, 28).

Preoperative clinically overt DIC in AA patients

Only few prospective studies published so far present incidences of preoperative, clinically overt DIC in patients with intact AA. Present data indicate that clinically overt DIC seems to be more frequent in patients with thoracoabdominal aneurysms than in patients with AAA and that persons with large and expanding aneurysms are especially prone for this coagulopathy.
Asymptomatic, compensated DIC

Compensated activation of the haemostatic system (phase I) in patients with AA, contrary to the clinically overt DIC (phase II and III), seems common and is probably underdiagnosed. In phase I of DIC, coagulation inhibitors restrict activation of haemostasis. Increased consumption of blood platelets and coagulation factors stimulate their synthesis. Therefore, in the assessment of compensated DIC global coagulation tests are of limited value (21, 27), specific markers of coagulation activation and haemostasis must be used. The compensated DIC can be recognized, even without bleedings, if appropriate laboratory tests are performed (27, 28). However, one marker does not suffice for the diagnosis of compensated DIC. According to Wada and associates (30) soluble fibrin monomer and fragment of crosslinked fibrin D-dimer have the highest specificity for DIC.

![Asymptomatic, compensated DIC](image-url)
Few publications focus on compensated activation of blood coagulation in patients with AA (2, 3, 5, 9, 16, 29, 31). Results summarised in Table 3 show the percent of AAA patients with abnormal coagulation parameters. Results differ from author to authors. They are related to varying cut-off values, aneurysm diameters, and exclusion criteria. In general, in AAA patients diminished platelet number is rare, diminished fibrinogen concentration scarce, but increased concentrations of different coagulation activation and fibrinolysis markers are common. The results of our study presented in Figure 1 show that by using the indicated cut off values for more than 30% of our AAA patients compensated activation of coagulation is characteristic.

Most of the precise tests of activation of coagulation (tissue factor, prothrombin fragment F1+2, thrombin-antithrombin complex, fibrin peptide A, soluble fibrine monomer) and fibrinolysis (plasmin-plasmin inhibitor complex) are laborious and expensive. Therefore, they are used for scientific investigation but not in routine work. Only the determination of D-dimer concentration is easily available for routine laboratory. Increased concentration of D-dimer indicates both fibrin deposition and degradation. In combination with other markers available in a specialized laboratory it documents the activation of coagulation, and enables to recognize compensated DIC.

In patients with AA and activated coagulation even a minor surgical procedure as angiography, can be complicated by extensive bleeding from the puncture site (14). During surgical repair of the aneurysm, the patient with compensated DIC (phase I) carries the risks typical for DIC: transition from phase I to phase II and III. Fatal results of this transition, occurring during or shortly after surgery, were described in patients with AA (11, 13, 17).

**Conclusion**

The recognition of preoperative activation of coagulation in patient with aortic aneurysm (phase I of DIC) seems to be very important. Macneily and Graham (14) recom-
mended additional determination of fibrinogen concentration and fibrin degradation products (besides platelets, prothrombin and partial thromboplastin time) in AA patients, in case of any suspicion of DIC. In our department each patient with AAA is suspected of intravascular activation of coagulation (compensated DIC). Therefore, before surgery besides basic coagulation tests, determination of D-dimer concentration and fibrinolytic activity in the whole plasma is always performed to select patients for preoperative anticoagulation treatment. This anticoagulation treatment resulting in diminishing preoperative abnormalities, decrease the probability of intraoperative transition from phase I of DIC to phase II and III and enables successful surgical aneurysm repair, which remains the definitive treatment of preoperative consumptive coagulopathy.

References