Effect of intraluminal thrombus on pressure transmission in the abdominal aortic aneurysm

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Objective: To clarify the effect of intraluminal thrombus on pressure transmission.

Methods: A saccular aneurysm was inserted into an artificial circulation system. Subsequently, the saccular aneurysm was filled with eight different human aortic aneurysm thrombus samples. Starch solution in an empty aneurysm was used as a control. A pressure sensor measured the pressure in the circulation, and a second piezoelectric sensor measured the pressure in the saccular aneurysm at 3, 2, and 1 cm from the endoluminal surface (23 locations). The influence of the elastic characteristics of the aneurysm wall on the extent of pressure reduction was evaluated by experiments performed with aneurysms made of rubber and paraffin.

Results: The pressures measured in the empty aneurysm were identical to those measured in circulation (P > .05). The pressure measured in the thrombus was significantly lower than the pressure measured in the circulation (P < .05). The mean pressure ratio between the systolic thrombus pressure and systolic circulation pressure at 1, 2, and 3 cm was 0.90 ± 0.09, 0.86 ± 0.10, and 0.81 ± 0.09, respectively. However, there was a clear correlation between the pressure in the circulation and in the thrombus (Pearson correlation coefficient: mean, r = .997; range, 0.975-0.999; P < .01). The change in circulatory pressure was followed by an almost identical change in thrombus pressure (regression coefficient: mean, β = .997; range, .983-1.000; P < .01). In stiffer aneurysms, the pressure reduction is less than in more compliant ones (P < .05).

Conclusions: In an in vitro model, pressure in the aneurysmal sac is reduced by fibrinous thrombus. (J Vasc Surg 2005; 42:1176–82.)

Clinical Relevance: Endovascular aneurysm repair (EVAR) aims at reducing the pressure in the aneurysmal sac. Therefore, it seems attractive to use pressure monitoring in the aneurysmal sac as a follow-up after EVAR. This study contributes to the development of the rationale of pressure monitoring in the aneurysmal sac as a follow-up method after EVAR. The aneurysmal sac is filled with thrombus. To interpret pressure measurements in the thrombus, we have to learn about the effect of the thrombus on pressure transmission and on the pressure measurements themselves. Our study demonstrates that reduction of pressure occurs as it is transmitted through a human aortic thrombus.

One of the most frequent complications after endovascular aneurysm repair (EVAR) is the occurrence of an endoleak or endotension. An endoleak is defined by the persistence of blood flow outside the lumen of the endoluminal graft within an aneurysm sac or an adjacent vascular segment being treated by the graft. In approximately 20% of patients treated by EVAR, an endoleak occurs sooner or later. Endotension is defined as a state of significant pressure in the aneurysm sac without any evidence of an endoleak as identified by imaging techniques. Computed tomography is considered the “gold-standard” for endoleak and endotension diagnosis. Disadvantages of this method are that it is expensive and time consuming and is associated with radiation. In addition, there are false-negative results because not all endoleaks can be visualized.

Both endoleak and endotension carry the risk of abdominal aortic aneurysm (AAA) rupture because of continuous or renewed pressurization of the sac. Because the goal of successful EVAR is to decrease intra-aneurysm sac pressure by excluding the aneurysm sac from the systemic circulation, it seems attractive to use pressure monitoring in the aneurysm sac as a follow-up after EVAR. However, continuous noninvasive pressure measurements are currently not available.

To determine whether intra-aneurysm sac pressure measurement can be used to diagnose the presence of endotension or endoleak and, possibly, to predict the risk of aneurysm rupture, it is necessary to investigate the effect of the intraluminal thrombus on pressure transmission. This effect on pressure transmission is still unclear.

The aim of this study was to clarify the effect of the intraluminal thrombus on the pressure transmitted from the endoluminal side of the thrombus toward the wall of the aneurysm. On the basis of previous pressure measurements during open surgery, we hypothesized that the pressure measured in the aneurysm is the same as the pressure measured in the systemic circulation and that the thrombus does not have a dampening effect on the pressure.

METHODS

In vitro model. An in vitro model of a saccular aneurysm (Fig 1) was inserted into an artificial circulation system to investigate the effect of the intraluminal thrombus on...
Saccular aneurysm model. The saccular aneurysms were made of elastic vulcanized rubber. The characteristics of the aneurysm walls of the various saccular aneurysms were constant. The aneurysms were successively filled with one of eight different human fibrinous thrombi obtained during aneurysm operations. The luminal part of the thrombus was always situated toward the circulation. The thrombus was wrapped tension free in the rubber aneurysm wall. These were glued together with silicone glue (Silicone kit; Bison International, Goes, The Netherlands) to prevent flow between the rubber aneurysm wall and the inserted human thrombus.

Validation aneurysm model. To validate the elastic properties of the aneurysm model with hardened silicone glue, the elastic modulus (Ep) was calculated within a physiological pressure range. The Ep, the ratio of pressure to strain, was calculated with the following formula:

\[
Ep = 133.3 \times \left[ \frac{\Delta P \times (D_1/D_2 - D_1)}{D_1} \right],
\]

where \(\Delta P\) is the change of pressure in the aneurysm model, \(D_1\) is the diameter of the aneurysm model at the lower pressure, and \(D_2\) is the diameter of the model at the higher pressure; 133.3 is a constant that converts \(Ep\) from millimeters of mercury to newtons per square meter.

Pressure inside the model was measured with a pressure catheter. The empty model was pressurized with water from 70 to 120 mm Hg, thus generating a pressure change of 50 mm Hg (\(\Delta P\)). The increase in aneurysm diameter was measured by two opposite laser scans (\(D_2 - D_1\)). The accuracy of the laser scan was 10 nm (Laser Head OFV-505, Controller OFV-5000; Polytec GmbH, Waldbronn, Germany). The data acquisition system Siglab 42 (Siglab, Bonn, Germany) was used. The change in diameter was measured by rotating the aneurysm model from 0° to 90° and, thus, was measured in two directions. In each position, the increase in diameter was measured three times.

Pressure measurements. Pressure measurements were performed by two pressure sensors (RADIAnalyzer PressureWire Sensor; RADI Medical Systems AB, Uppsala, Sweden). The commercially available coronary PressureWire has a 3-cm-long radiopaque platinum floppy tip. The radiopaque tip was snipped off beneath the sensor to enable precise placement of the sensor in the thrombus. According to RADI Medical Systems, shortening of the radiopaque tip did not influence the accuracy of the sensor.

Experiments. The saccular aneurysm was situated in a closed box connected to the circulation model. The pressure inside this box was kept at 12 mm Hg, the physiological abdominal pressure. The pulse rate of the circulation model was kept at 70 beats per minute during the experiments.

Pressure measurement inside the saccular aneurysm was performed at three different locations and with different systemic blood pressures, as illustrated in Fig 1. The PressureWire was inserted through a 21-gauge needle in the saccular aneurysm, followed by withdrawal of the needle over the PressureWire. The pressure measurements were performed at 3, 2, and 1 cm from the endoluminal surface. In this way, it was possible to study the influence of the thrombus on the pressure transmission, because the direction of the force generated by the pressure of the circulation was constant. One test was performed on a saccular aneurysm model without thrombus as control, so a pressure change caused by factors other than the human thrombus was excluded.

The systemic blood pressure was changed from a low blood pressure to a high blood pressure to mimic multiple in vivo situations. The systolic pressure range was 80 to 160 mm Hg, and the diastolic pressure range was 40 to 120 mm Hg, with pulse pressures varying from 30 to 50 mm Hg.

One pressure sensor measured the pressure in the circulation at the same location during the entire experiment, and the second pressure sensor measured the pressure in the thrombus at the same time. Two measurements inside thrombus 3 were performed, because the length of this thrombus was 2 cm instead of 3 cm. In this way, the systolic and diastolic pressure in all the different thrombi were measured at 23 locations in the thrombus.

First, the pressure catheter was introduced in the thrombus at 3 cm from the endoluminal surface (P3; Fig 1). Next, the catheter was introduced at 2 and 1 cm from the endoluminal surface (P2 and P1, respectively, Fig 1). Therefore, the effect of a needle track on the pressure measurements was excluded, because the pressure measurements were performed in front of the needle track of the previous measurements without disturbing any thrombus.

Before insertion of the pressure catheter into the thrombus, the sensor was calibrated in saline solution. When the catheter was introduced into the thrombus, the circulation was turned off. After the sensor was introduced into the thrombus, the readout was recorded at an atmospheric box pressure. The pressure sensor of the circulation and the pressure sensor in the thrombus were again adjusted to 0 mm Hg with the aforementioned box pressure of 12 mm Hg.

Statistical analysis. The systolic and diastolic pressures measured in the circulation and in the thrombus were compared statistically by means of a Wilcoxon signed rank test to evaluate the difference between two groups in paired
samples. Statistical significance was defined as a \( P \) value of \(<.05\). The Pearson correlation coefficient was used to determine whether there was a linear correlation between the systolic or diastolic pressure in the circulation and in the thrombus. A one-tailed test was used because we expected a positive correlation between the pressure in the circulation and the pressure in the thrombus; in other words, we expected that the pressure in the thrombus would increase if the pressure in the circulation were raised. The standardized regression coefficient was used to determine the change of systolic or diastolic pressure in the thrombus caused by an increasing systolic or diastolic pressure in the circulation. The agreement between the pressure in the circulation and the pressure in the thrombus was depicted in a scatter plot.

To investigate the influence of the stiffness of the aneurysm wall on the pressure transmission in the thrombus, we measured the pressure on \( P_1, P_2, \) and \( P_3 \) as previously described in a rubber aneurysm model with an \( Ep \) identical to that of an AAA. This rubber aneurysm model was then molded in paraffin. The wall of the model was totally rigid so that we could compare an extreme situation with the physiological one. Pressure measurements were performed again on \( P_1, P_2, \) and \( P_3 \) and are called \( PP_1, PP_2, \) and \( PP_3 \). The ratios between the pressure measured in the thrombus and the pressure measured in the circulation were calculated for \( P_1, P_2, P_3, PP_1, PP_2, \) and \( PP_3 \). The ratios of the rubber model were statistically compared with the ratios of the pressure measurements in the same place in the paraffin model by using the Mann-Whitney test. Statistical significance was defined as a \( P \) value of \(<.05\). The ratios were depicted in a box plot.

Pressure measurements were performed by a mean systemic pressure of 80 to 120 mm Hg. For statistical analysis, SPSS 11.0 for Windows was used (SPSS Inc, Chicago, Ill).

RESULTS

The data from the validation experiments of the aneurysm model are listed in the Table. The mean \( Ep \) of the aneurysm model with hardened silicone glue without thrombus was 36 N/cm\(^2\). The standard deviation was 1.57 N/cm\(^2\).

The pressure readout after the introduction of the catheter into the thrombus was variable. The mean readout at \( P_1, P_2, \) and \( P_3 \) after catheter introduction was 5 ± 5 mm Hg, 4 ± 7 mm Hg, and −1 ± 8 mm Hg, respectively. Figure 2 depicts the pressure readouts after sensor introduction into thrombi 1 to 8.

The pressure measured at \( P_1, P_2, \) and \( P_3 \) (Fig 1) in the aneurysms, which were filled with the eight different human fibrinous thrombi samples and once with the starch solution as a control, was compared with the pressure measured in the circulation by means of Wilcoxon signed rank tests. The pressure measured in the circulation and the pressure measured in the empty aneurysm (filled with starch solution) were, as expected in this control, identical (\( P > .05 \)). Our hypothesis that the pressure measured in the thrombus would be the same as the pressure measured in the circulation was rejected (\( P < .05 \)) in all experiments. The systolic pressure ratio (mean ± SD) between the systolic thrombus pressure and the systolic circulation pres-

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**Table.** Data of validation of aneurysm model

<table>
<thead>
<tr>
<th>Position</th>
<th>Measurement</th>
<th>( \Delta P ) (mm Hg)</th>
<th>( D_1 ) (cm)</th>
<th>( D_2 ) (cm)</th>
<th>( Ep ) (N/cm(^2)) *</th>
</tr>
</thead>
<tbody>
<tr>
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<td>50</td>
<td>1.580</td>
<td>1.611</td>
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<td>50</td>
<td>1.580</td>
<td>1.610</td>
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<tr>
<td></td>
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<td>1.580</td>
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<tr>
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</tr>
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\( D_1 \), diameter of the aneurysm model at the lower pressure; \( D_2 \), diameter of the model at the higher pressure; \( Ep \), elastic modulus.

*Mean ± SD, 36 ± 1.57 N/cm\(^2\).*
sure at P1, P2, and P3 was 0.90 ± 0.09, 0.86 ± 0.10, and 0.81 ± 0.09, respectively, and the diastolic pressure ratio (mean ± SD) between the diastolic thrombus pressure and the diastolic circulation pressure was 0.88 ± 0.07, 0.85 ± 0.08, and 0.81 ± 0.10, respectively.

The agreement between the pressure measured in the circulation and the pressure measured at P1 (red triangles), P2 (green squares), and P3 (blue triangles) in thrombus 1 at varying systemic pressures is shown in Figs 3 and 4. The 46 scatter plots of all the experiments performed with the other thrombi were identical to the scatter plot of thrombus 1. The plots showed that the pressure measurements were situated beneath the reference line. The black reference line represents the situation in which the measured pressure in the circulation is equal to the pressure in the thrombus. Figure 5 depicts the ratios of all thrombi between the pressure in the thrombi at P1, P2, and P3 and the pressure in the circulation.

The correlation between the systolic or diastolic pressure in the thrombus and the systolic or diastolic pressure in the circulation was statistically significant (mean r = 0.997; range, 0.975-0.999; P < .01). The mean standardized regression coefficient between the systolic or diastolic pressure in the thrombus and in the circulation was β = 0.997 (range, 0.983-1.000; P < .01).

The ratios between the pressure in the thrombus and the pressure in the circulation of the rubber aneurysm model were significantly different from the ratios of the paraffin aneurysm model (P < .05; Fig 6). The pressure ratio (mean ± SD) at P1, P2, and P3 was 0.96 ± 0.02, 0.89 ± 0.01, and 0.67 ± 0.01, respectively, and at PP1, PP2, and PP3 it was 0.98 ± 0.01, 0.93 ± 0.01, and 0.86 ± 0.02, respectively.

**DISCUSSION**

Surveillance of the aneurysm sac pressure could be a follow-up method after EVAR, because endoleaks and endotension are associated with an increased aneurysm sac pressure. To determine whether continuous intra-aneurysm sac pressure measurements can be used to diagnose the presence of an endoleak or endotension, it is necessary to investigate the influence of the intraluminal thrombus on pressure transmission.

This study demonstrates that both the diastolic and systolic pressure are reduced by human fibrinous thrombus. We decided to investigate the systolic and diastolic pressure only, because the pulse and the mean pressure are resultants of the systolic and diastolic pressure. All 46 scatter plots of the experiments showed that the lines of the measured systolic and diastolic pressure were situated beneath the pressure measurements under control conditions. This means that the measured systolic and diastolic pressures in all thrombi were lower than the measured systolic and diastolic pressures in the circulation. The ratios between the thrombus pressure and the circulation pressure varied from thrombus to thrombus and depended on the distance from lumen to sensor (Fig 5).

During analysis of the scatter plots, it became clear that the distance between the pressures at P1 and P2 was different from the distance between the pressures at P2 and P3 (Figs 3 and 4). This implies that the decrease of pressure between P1 and P2 was not equal to the decrease of pressure between P2 and P3, whereas the length of the thrombus was the same. This phenomenon can probably be explained by the inhomogeneity of the thrombus. Vallabhahreni et al have reported this phenomenon before.
discovered a significant variation in the pressure recorded within aneurysm thrombi in different patients and within the same aneurysm. Image analysis of the thrombus revealed a significant variation in matrix density that correlated with the variation in pressure transmission. A possible misleading factor of this study is that the pressure measurements in the thrombus at P1, P2, and P3 were performed not at the same time, but successively; however, they were performed under the same conditions.

Because pressure reduction depended on the distance from lumen to sensor and because various thrombi had different pressure-reduction specifications, it seems difficult, if not impossible, to accurately measure pressure in the entire sac at a single location. Stable high pressures need reintervention, and stable low pressures do not. However, the cutoff point between high and low aneurysm sac pressures will stay a subject of discussion.

A pressure trend is probably most appropriate to follow. This is supported by our data, in which a change in pressure in the circulation caused an almost identical change in pressure in the thrombus despite differences between thrombi. A pressure increase will be associated with an unsuccessful EVAR, and a pressure decrease, with a successful EVAR.

The presented aneurysm model is probably the optimal reflection of the real situation. The elastic property of our rubber model with silicone glue was identical to the elastic property of an AAA. The mean Ep of AAAs is 31.3 N/cm² (range, 10-80 N/cm²). The Ep of our aneurysm model was 36 N/cm². Our aneurysm models were filled with fibrinous thrombi obtained during aneurysm operations. Of course, it was not possible to simulate the biological changes of thrombi that take place in vivo after EVAR.

The elastic property of the aneurysm wall might influence the pressure in the thrombus. To determine the effect of human aortic thrombus on the pressure transmission, the elastic property of the aneurysm wall was kept constant during the experiments performed with the eight different thrombi (Ep = 36 N/cm²). During the last experiment, it became clear that the reduction of pressure in a thrombus is dependent on the elastic property of the aneurysm wall. Thrombus still reduces pressure in a rigid paraffin model, but the extent of reduction is less than in a more elastic rubber model. This means that pressure reduction by fibrinous aneurysm sac thrombus will also take place in vivo, because the range between the Ep of the rubber aneurysm model and the Ep of the paraffin aneurysm model includes the physiologic one.

After calibration of the pressure sensor in saline solution, we introduced the catheter into the thrombus and recorded the readout. After introduction of the sensor into the thrombus, we again adjusted the sensor to 0 mm Hg. In this way, it was possible to measure the relative pressure change between the systemic pressure in the circulation and the pressure in the thrombus. This is different from clinical aneurysm sac pressure measurements. In our opinion,
al,8 and Wang et al9 also determined in a computer model measurements of the intraluminal thrombus and of the abdominal-thrombus acts as a mechanical buffer, by compliance measurement. The mean readout after introduction of the catheter into the thrombus was variable during our experiments (Fig 2). The pressure readout after catheter introduction in the thrombus was 5, 4, and 1 mm Hg, respectively, and the range was −3 to 13 mm Hg, −6 to 16 mm Hg, and −7 to 14 mm Hg, respectively. Theoretically, it is possible to measure a false pressure signal caused by bending stress on the wire. The solid thrombus could influence the pressure on the membrane of the sensor. The pressure readout after catheter introduction in the thrombus should be 0 mm Hg, because the thrombus was wrapped tension free in the rubber aneurysm wall and one side of the saccular aneurysm was open. If a positive or negative pressure occurred inside the thrombus, the thrombus should either expand or shrink.

In the literature, several investigations into the effect of thrombus on pressure transmission have been performed. Our findings on intrathrombotic pressure are compatible with the results of Vorp et al. They concluded that the thrombus acts as a mechanical buffer, by compliance measurement. The intraluminal thrombus and of the abdominal aortic wall. Inzoli et al,6 Di Martino et al,7 Mower et al,8 and Wang et al6 also determined in a computer model that thrombus reduced aneurysm wall stress. In these studies, no real-time pressure measurements were performed.

Data from studies using fluid-filled needles for pressure measurement suggest that in some cases, thrombus does reduce pressure.16 Because the most common problem with fluid-filled needles is needle obstruction, resulting in falsely low readings,16 the literature is quite unclear about thrombus and pressure reduction. We concluded in collaboration with Dias et al21 that the RADI PressureWire is a reliable and reproducible technique for measuring pressure within the aneurysm sac thrombus. Although the problem of a fluid-filled sensor is sensor obstruction, which yields falsely low readings, Hans et al12 and Schurink et al13 concluded with the use of fluid-filled pressure devices that thrombus does not reduce pressure. This difference could be explained by the moment of zeroing the pressure sensor. As mentioned, we adjusted our sensor to zero after introduction of the sensor into the thrombus, so artifacts caused by bending stress on the sensor were excluded. We understand that this is not possible in vivo experiments.

Our findings correspond with the conclusion of the study performed by Pacanowski et al.14 They determined in an in vitro model that thrombus resulted in decreased transmission of pressure to the arterial wall. The pressure distribution was also uneven. Pressure in this study was measured by pressure-calibrated strain gauges (non-fluid-filled sensor). Thrombus was created by injection of thrombin into the aneurysm sac. Fibrinous thrombus obtained during open surgery was not investigated.

Adolph et al15 observed that thrombus within the aneurysm contains fissures and canaliculi that are fluid permeable, so the intraluminal pressure in the AAA is the same as the pressure in the wall of the aneurysm. This is an indirect conclusion (no pressure measurements were performed). Their main purpose was not to investigate the role of thrombus in pressure transmission. Rather, they investigated whether thrombi have significance in the pathophysiologic mechanism of AAAs.

In conclusion, our study demonstrates a reduction of pressure as it is transmitted through a human aortic thrombus. The extent of reduction depends on the elastic properties of the aneurysm wall. This implies that caution is required for the interpretation of the measured pressure level. In this in vitro study, pressure measurement with one sensor in the aneurysm sac seems appropriate to determine pressure changes in the entire aneurysm sac. Because pressure reduction occurs through the thrombus and this reduction depends on the thrombus itself, on the elastic property of the aneurysm wall, and on the distance from lumen to sensor, it seems difficult to make predictions about the entire sac based on pressure measurement in a single location. A pressure trend seems more appropriate to follow than the absolute intrasac pressure. Further research is necessary to determine other potential artifacts and problems with pressure monitoring in the aneurysm sac that might explain variation between studies and between patients.

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Fig 6. Ratios between the pressure in the thrombus and the pressure in the circulation. Measurements were performed in the same thrombus in a rubber aneurysmal model (PP1, PP2, and PP3) and a paraffin aneurysm model (PP1, PP2, and PP3). Median, 25th and 75th percentiles, and range are shown.
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REFERENCES


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