Aortic wall structural strengthening by intraluminal net prosthesis to arrest aneurysm progression and to prevent dissection and rupture

Abstract The major limitation implicit in the endovascular procedures for aortic prosthetic substitution is that they cannot be used in those tracts of the aorta where important collateral branches originate (aortic arch, thoraco-abdominal tract, upper abdominal), that would be occluded by the prosthesis. In order to overcome this limitation we hypothesized the endovascular positioning of a prosthesis in the form of a wide mesh network that would be gradually and spontaneously covered by new intima and included in the aortic wall. The fabric framework linked to the aortic wall would then condition its significant, regular and uniform mechanical strengthening that fractionates and partially absorbs the centrifuge pulsatile stress of the bloodstream. The purpose of this paper is to report the results of the insertion of a braided Prolene net prosthesis in the first 7 cm of the descending aorta of ten swine. The animals were killed after 6 weeks, the substituted segment removed and aortic wall compliance measured under standardized conditions. The prosthesis was found entirely covered by new intima, well embodied in the aortic wall. The intercostal collateral included in the substituted segment was patent, as proved by bubble formation during underwater insufflation. Compliance of the prosthesis segment was significantly lower than that of the adjacent descending aorta. Histology showed a regular net prosthesis inclusion deep in the neo-intima layer. Present results indicate the technical feasibility of the procedure, achieving significant aortic wall strengthening without affecting the collateral (intercostal) circulation.

Keywords Aneurysm • Dissection • Thoracic aorta • Marfan’s disease

Introduction

Prosthetic substitution of thoracic and abdominal aortic aneurysms has recently been successfully accomplished by endovascular techniques, avoiding thoracotomy or laparotomy [4, 11, 12, 14] (Fig. 1). These techniques are still at an experimental phase and significant improvements in the devices are probably required before they can gain wide acceptance. However, the major limitation implicit in these procedures is that they cannot be used in those tracts of the aorta where important collateral branches originate (aortic arch, thoraco-abdominal tract, upper abdominal), since these would be occluded by the prosthesis. On the other hand it is the prosthetic substitution of these very aortic segments that is associated with the highest risk of complication.

In the pathogenesis of aneurysm, acquired or congenital diseases induce modifications of the vascular wall, often resulting in depauperation of elastic fibers [20] that cause its gradual inability to withstand the blood pressure, so that dilatation slowly occurs and gradually progresses to the point of eventual rupture or dissection [16]. The relative slowness of aneurysm formation and progression to
rupture indicates that the decrease in the strength of the arterial wall under the aneurysm formation threshold may be very gradual and limited; consequently one can imagine that measures to increase, even moderately, the mechanical strength of the arterial wall should be successful in arresting aneurysm progression and preventing rupture.

As a possible means of realizing such arterial wall strengthening, we hypothesized the percutaneous insertion into the aortic lumen of a prosthesis formed out of a net of braided Prolene, fitted with a co-axial stainless steel thin coil to provide stable contact with the vascular wall. The rationale is that the net prosthesis maintained in contact

![Fig. 1](image1.png)

Fig. 1 The major limitation of the endovascular procedures for aortic prosthetic substitution [4, 12, 14] is that they cannot be used in those tracts of the aorta where important collateral branches originate (aortic arch, thoraco-abdominal tract, upper abdominal), since these would be occluded by the prosthesis. On the other hand, it is the prosthetic substitution of these very aortic segments that is associated with the highest risk of complications (modified from 14).

![Fig. 2 A, B](image2.png)

Fig. 2A, B The experimental hypothesis is based on the fact that the net prosthesis together with the steel coil, positioned with endovascular techniques and maintained in contact with the aortic walls (A) is gradually covered by the neo-intima (B) and invaded by fibroblasts, and thus stably associated to the aortic wall. If the net mesh is properly dimensioned, it may be expected that the blood flow through the collateral branches is not affected (arrows).

![Fig. 3](image3.png)

Fig. 3 The aortic wall-linked fabric framework would condition a significant, regular and uniform mechanical strengthening that fractionates and partially absorbs the centrifugal pulsatile stress of the bloodstream, thus preventing dilatation and intimal tear, which is the first, necessary pathogenic event of dissections as well as, at least in most cases, of rupture. From the strictly mechanical point of view, the effectiveness of this modality of structural strengthening is witnessed by its wide application in current use items (i.e. gardening rubber tubes, tires etc.), where a tubular elastic material (i.e. rubber) is reinforced by means of a more rigid material framework (i.e. fabric, steel wire, etc.). The structural properties of the aortic wall associated to the intraluminal net prosthesis should result from the combinations of three factors: 1 the structural properties of the net prosthesis, 2 the structural properties of the aortic wall, 3 the strength of the bonds between the aortic wall and the net prosthesis.
with the intimal wall (Fig. 2 A) would be gradually covered by new intima, invaded by fibroblasts and then stably associated to the aortic wall (Fig. 2 B). The fabric framework linked to the aortic wall would then provide a significant, regular and uniform mechanical strengthening that fractionates and partially absorbs the centricpulsatile stress of the bloodstream (Fig. 3).

From the strictly mechanical point of view, this modality of structural strengthening is similar to that largely employed in currently used items (i.e. gardening rubber tubes, tires etc.), where a tubular elastic material (i.e. rubber) is reinforced by means of a more rigid material framework (i.e. fabric, steel wires, etc.). Of course the only reason to prefer arterial wall net prosthesis strengthening versus standard prosthetic conduit substitution is that the former may be expected not to interfere with the blood flow through the collateral branches. This could then extend the very significant advantages of the endovascular techniques to the entire aorta, including the aortic arch.

The purpose of the study is to demonstrate the experimental hypothesis that significant strengthening of the aortic wall, theoretically capable of arresting aneurysm progression and preventing rupture, can be achieved by a net prosthesis that can be positioned with an endovascular technique without interfering with blood perfusion of the collateral branches.

Materials and methods

Experimental model

A preliminary simulation model was assessed with PVC transparent tubing to evaluate wall adherence of the various mesh net shapes and types in water flow, both in straight and in fusiform conduits. In these preliminary experiments we found that adhesion of the net to the tube wall relying only on the effect of the water flow was far from constant and regular, even with modified fluid-dynamic shapes of the net mesh. After a few endeavors, the problem was perfectly solved by a thin stainless steel coil co-axial to the net prosthesis. The coil allowed a constant and stable contact of the prosthesis net with the wall, also in fusiform conduits. Moreover, the mechanical properties of the coil added further strength to the aortic wall and also served to collapse the prosthesis during insertion. The net prosthesis used has a roughly rhomboid mesh (approximately 1 x 1 mm wide) of braided Prolene®; it was prepared as a cylindric conduit, fitted with the stainless steel coil (wire diameter 0.3 mm, AISI 304), immediately before implant, in a diameter only slightly exceeding that of the first tract of descending aorta of the animal.

The steel-and-polypropylene net prosthesis was positioned in the first 7 cm of the descending aorta of ten swine (25-40 kg); the contracted coil and the prosthesis were quickly inserted through a brief transverse aortotomy at the proximal end of the clamped descending aorta, without bypass or extracorporeal circulation. A single low dose heparin (100 UI/kg, i.v.) was given during the operation. No anti-aggregant and/or anticoagulant medications were given in the postoperative period. The animals were killed after 6 weeks.

Measurements and analysis

At animal sacrifice the descending aorta with the net prosthesis was sampled together with the confining distal aortic segment of equal length. To verify the patency of the collateral branch in the net prosthesis segment, this was inflated at low pressure (<40 mmHg) and examined underwater looking for bubble formation.

To evaluate the effects of the steel-and-polypropylene net prosthesis on dilatation of the aorta, under standardized conditions the circumferences of the prosthesis segment at two pressures (40 and 100 mmHg) were compared with those recorded in the aortic segment immediately distal; from these values the compliance of the respective unitary vascular cylinder can also be calculated. A stress test of the bonds between the prosthesis and the aortic wall was carried out by generating 300 mmHg pressure for 10 min in the net prosthesis aortic segment. That was then longitudinally opened and carefully examined for macroscopic evidence of detachment area of the prosthesis from the vascular wall.

Histology of the prosthetic segment was carried out.

Results

The prosthesis positioning was very simple with a very short clamping time (5 min); all animals survived the procedure without detectable neurological deficit.

Three out of ten animals died on the 3rd, 17th and 32nd postoperative day, respectively. Left hemithorax empyema was the cause of the third death; in the other two thrombo-

Fig. 4 The prosthesis consists of a close-mesh net of braided Prolene fitted with a co-axial thin stainless steel coil to enhance regular and uniform contact with the vascular wall (left). To simplify this research phase the prosthesis was positioned with open technique, although it is devised to be positioned through a peripheral vessel (transfemoral) as an entirely endovascular procedure. After 6 weeks the net prosthesis was found to be entirely covered by the new intima and well attached to the aortic wall. In the right side of the prosthesis segment (middle) the net is no longer visible; presumably with more time this smooth intimal surface would extend to the whole inner vascular surface (middle the aortic wall was sectioned with the coil in place, right the metallic coil was pulled out).

Fig. 5 To test patency of the thin collateral branch, before opening the aortic segment was inflated with air at 40 mmHg and examined underwater. Bubble formation confirms the patency of the intercostal branch in the net prosthesis segment (left, arrows). The net prosthesis was then detached from the aortic wall and examined by transillumination. The newly formed intimal cylinder is clearly visible filling the mesh net framework throughout the prosthesis. The absence of the new intima to fill the prosthetic segment, this was inflated at low pressure (<40 mmHg) and examined underwater looking for bubble formation.

Fig. 6 A, B Histology shows a very thick neo-intima layer completely including the net prosthesis which lies in contact with the media. The square area shows the enlarged polypropylene mesh net pattern

1 Ethicon, Somerville, NJ 08876-0151, USA

2 The swine strain provided to our lab (Large White) has a constant unique collateral branch in the first tract of the descending aorta, supplying the bronchial systemic circulation [13]
blood flow interruption phase, which may be considered no longer required. However, a theoretically even more important advantage, at least in thoracic aorta prosthetic substitution, lies in the fact that laparotomy and thoracotomy is of patients. The most obvious advantage of these procedures lies in the fact that laparotomy and thoracotomy is no longer required. However, a theoretically even more important advantage, at least in thoracic aorta prosthetic substitution, is that the endovascular techniques avoid the blood flow interruption phase, which may be considered the most important cause of complications, direct or indirect, of the standard, open technique. In fact, directly proportional to the duration of cross-clamping is the risk of ischemic lesions to distal organs (liver and kidney) as well as that of paraplegia from spinal cord injury [3]. Indirect complications of blood flow interruption are those related to the use of bypass, shunts, extracorporeal circulation, spinal cord drainage, nitroprusside and other maneuvers [1, 7, 10, 18] often established to provide distal perfusion and/or to compensate the upper body area for hemodynamic changes induced by clamping; the complications of systemic heparinization, usually required by these techniques, are thus also indirectly dependent on blood flow interruption.

As emphasized before, standard prosthetic conduit positioning by endovascular techniques is possible only in those aortic segments without important collateral branches (upper descending thoracic and infrarenal abdominal aorta). The design of the prosthesis as a wide-mesh net is then intended to extend the significant advantage of the endovascular techniques to all the aortic segments. In this regard, the final question to be answered to validate the possible clinical use of the net prosthesis, of course, concerns the entity of structural strengthening provided to the diseased aortic wall by these means.

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Table 1 Aortic wall compliance

As emphasized before, standard prosthetic conduit positioning by endovascular techniques is possible only in those aortic segments without important collateral branches (upper descending thoracic and infrarenal abdominal aorta). The design of the prosthesis as a wide-mesh net is then intended to extend the significant advantage of the endovascular techniques to all the aortic segments. In this regard, the final question to be answered to validate the possible clinical use of the net prosthesis, of course, concerns the entity of structural strengthening provided to the diseased aortic wall by these means.

The final structural properties of the aortic wall associated to the intraluminal net prosthesis may be complex to analyze in detail but, theoretically, should result from the combination of three factors (Fig. 3):

1. the structural properties of the net prosthesis,
2. the structural properties of the aortic wall,
3. the strength of the bonds between the aortic wall and the net prosthesis.

From a practical point of view, however, the clinical use of such a prosthesis could be justified if each of these factors were proved individually to be able to withstand the forces occurring physiopathologically within the vascular lumen.

Concerning the first factor, structural analysis showed that an ideal polypropylene net prosthesis with squared mesh 5 × 5 mm with a thread diameter of 0.5 mm sustaining a pressure of 300 mmHg (0.04 N mm⁻²) is charged at 50% of its failure tension (Fig. 7), thus guaranteeing the linear elastic behavior of the polypropylene. This computation was carried out considering only the transverse threads, assuming they entirely support the circumferential stress, ignoring the mechanical contribution of the longitudinal threads and that of the steel wire; it is then obvious that this theoretical prosthesis, which is much weaker and with wider meshes than that used in this experimental series, is certainly able to support forces largely exceeding those occurring within the vessels, even in pathological conditions.

Concerning the second factor, i.e. the aortic wall structural properties, it is obvious that they are impaired by the
The simplified mechanical model represented here is set up under the hypothesis of membrane behavior for thin cylindrical pipes [21] and regular geometric conditions. The average value of the stress in the net prosthesis and inside the artery wall is evaluated assuming a square mesh of the net made of threads arranged along the longitudinal and transverse directions of the blood vessel. The stress level in the artery wall can now be examined considering the cylindrical part of length \( l \) included between two contiguous transverse threads as indicated in B. This part can be easily idealized as undergoing both the circumferential stress \( \sigma_c \) and the longitudinal stress \( \sigma_l \). Consistent with the previous hypothesis, the entire load can be attributed to the transverse threads only, ignoring the stiffening effect of the circumferential stress. The whole carry- ing capacity of the single strip is ascribed to the presence of the longitudinal stress \( \sigma_l \). Therefore, the strip of blood vessel between two adjacent transverse threads is idealized as a plane membrane of indefinite length and width \( l \), supported along the edges as shown in B. Considering now the values of the elastic moduli of the two materials [5, 6, 22, see below], polypropylene and aorta wall, the ratio \( E_f/E_i \), is always greater than 2500. That leads to the observation that the threads can be considered inextensible when compared to the flexibility of the wall of the blood vessel. In the described situation the average value of the stress in the aorta wall is \( \sigma_i = 0.0421 \text{ N mm}^{-2} \). This stress can be compared to the average stress obtained in the normal condition of the aorta, without any reinforcement. Applying the relation \( \sigma_i = pr \), often named law of Laplace, where \( r = 2.5 \text{ mm} \) is the thickness of the vessel wall and \( \sigma_i \) is now the average stress in the thickness of the aorta wall, the internal stress of the aorta without reinforcement is \( \sigma_i = 0.224 \text{ N mm}^{-2} \), approximately 5 times greater than the value obtained for the reinforced wall. Formulas: \( P = 2pr \) (artery pressure resultant), \( F = \sigma Ap \) and \( F = Pl = 2prl \) (force carried by each thread). Symbols: \( P \) (artery pressure) = 300 mmHg = 0.04 MPa; \( r \) (equivalent radius of the blood vessel) = 14; \( l \) (transverse thread distance); \( \phi \) (thread diameter) = 5 mm; \( \sigma_i \) (admissible stress in the thread); \( A_p \) (cross-section of the thread). Elastic moduli of the materials: Polypropylene: \( E_f = 1200 \text{ MPa} \); Aorta, intima-media layer, pig: \( E_f = 447.5 \text{ KPa (ascending aorta)}, E_f = 43.25 \text{ KPa (thoracic aorta)}, E_f = 247.8 \text{ KPa (descending aorta)} \). Underlying disease to the extent that aneurysmatic dilatation has already occurred. Nevertheless, it can be assumed that the fractionation in sectors operated by the net prosthesis framework on the aortic wall allows for a significant increase in its ability to withstand the same intravascular pressure, in each of these sectors, with reduced dilatation. Structural computation indicates that, with the net fractionation provided by the theoretically ideal prosthesis (see above), the wall stress is 5 times lower in these sectors than in the aortic wall without the prosthesis (Fig. 7). Thus it can be reasonably expected that this significant strengthening would be sufficient to compensate the pathological changes induced by the underlining primary disease and, consequently, to prevent further dilation at the sectors of the wall delimited by the meshes threads.

As the prosthesis is positioned intraluminally, the critical point of this model could be the strength of the bonds between the prosthesis and the aortic wall, established essentially by neo-intima coverage and fibroblastic invasion of the prosthesis fabric. A pressure of 300 mmHg for 10 min was unable to cause any macroscopical and microscopical evidence of the breaking of these bonds and detachment of the prosthesis from the intimal layer. Although this result could not be automatically extended to prostheses with other configurations, for example with wider meshes, nonetheless it speaks in favor of the ability of these bonds to withstand the forces present within the vascular lumen, even in pathological conditions.

The expected mechanical effects of the net prosthesis at the intima level deserve special consideration. The permanence of the prosthesis in contact with the vascular wall in fact stimulates neo-intima formation that doubles its thickness, several times, thus making a new intimal cylinder that, with the mesh size used in this experimental series, is continuous, entirely including and covering the prosthesis (Fig. 4, 5). This newly formed intimal cylinder, strengthened by the prosthesis framework in the ideal position at this level, allows for a particularly effective action in preventing the formation and extension of intimal tears. Since intimal tear is the first and necessary pathogenic event of aortic dissection of all types [2] it is easy to anticipate an important clinical impact in the prevention of this complication of aneurysm. On the other hand, this selective intimal strengthening should also have a clinical impact on full thickness aneurysm rupture/fissuration mechanism by providing, with the neo-intima cylinder and steel-and-polypropylene prosthesis framework, the first and most active barrier. In other words the final goal of this net prosthesis, i.e. prevention of aneurysm rupture and/or dissection, may be the result, on the one hand, of the stabilization of the aneurysm diameter [16] and, on the other, of the increased resistance to lacerations of the intimal layer, significantly strengthened by its increased thickness and by the prosthesis network.

A two-fold mechanism leading to aortic dissection and rupture has recently been emphasized by Robicsek and Thubrikar [16]. They hypothesized that in Marfan’s disease the aortic enlargement combined with the decrease in wall thickness causes, according to the Laplace law, the stress to increase approximately as a square of the radius, and this is then the leading cause of rupture. In hyperten-
Circumferential Stress ($S_c$)

\[
S_c = \frac{PR}{T}
\]

**Aortic wall thickness ($T$)**

**Fig. 8** Variation of the circumferential stress through the arterial wall thickness. For a thick cylinder (thickness >8% of the radius ($R$)) such as the aorta, the stress is not uniform throughout the wall; it is maximal on the inner wall, decreases through the thickness of the wall and is minimal on the outer wall. This may explain the pathogenetic mechanism of dissection, where only the inner wall tears; moreover it adds arguments to the rationale of intraluminal positioning of the net prosthesis in order to achieve the structural strengthening just where this is most needed, i.e. where the circumferential stress is maximal. This allows for the required strengthening with the lowest amount of prosthetic material (thinner threads) (modified according to Robicsek and Thubrikar, Ann Thorac Surg 1994; 58:1247-1253)

**Fig. 9A, B** These schematic sketches represent examples of the possible net prosthesis-steel coil configuration in place, in two of the highest risk clinical conditions, i.e. aortic arch (A) and descending aorta aneurysm (B), where cross-clamping substitution must face the very low tolerance to normothermic ischemia of the nervous tissue. Spinal cord (paraplegia) and brain damage are the dreadful complications of open procedure repair, largely unpredictable even in the presence of sophisticated protective maneuvers. Aortic wall strengthening provided by the newly formed intimal cylinder and the polypropylene meshes and steel coil framework, as shown in the figures, should be theoretically able to withstand forces largely exceeding those usually present in the vascular lumen, even in pathological conditions without impairing the collateral circulation.

The results of this preliminary study clearly indicate the technical feasibility of the procedure without affecting the collateral (intercostal) circulation. The increase of mechanical resistance of the aortic wall fitted with the steel-and-polypropylene prosthesis is very important and, in accordance with the structural analysis, largely exceeds that required to hypothesize a real clinical meaningfulness. Obviously further tests under many different experimental conditions are required to assess other factors involved in this new therapeutic hypothesis.

One of the most important factors concerns the possible unfavorable effects of debris, thrombus, calcifications, arteriosclerosis and necrotic material on the net prosthesis neo-intima coverage and fibroblastic invasion and thus, ultimately, on the prosthesis-aortic wall linkage. This event, which the present experience has shown to occur regularly in the normal aorta, is of course the condition necessary to produce the expected mechanical effects and thus any impairment to this linkage may have an important clinical impact. An essential requirement for realizing this linkage, experimentally already directly verified in our preliminary work, is the uniform and stable contact of the prosthesis with the aortic wall. In this regard the deformation and irregularity of the aneurysmatic lumen shape may cause some problem. It may be noticed, however, that the often spontaneous thrombosis of the more peripheral area of the aneurysm provides a trend towards reduction and rectification of the aneurysmatic lumen, thus creating conditions more favorable to net prosthesis-vascular wall contact.

The ideal dimensions of the mesh of the prosthesis, as well as of the fabric thread that provides the best structural vascular wall reinforcement with the lowest interference with the orifices of the collateral branches, is an other important point which must be investigated in detail. The present experience has proved to us that the patency of the small intercostal branch can be achieved, at least for 6 weeks, in spite of the quite close-mesh net, with vigor-
ous neo-intima proliferation. This is due to the fact that neo-intima can fill the narrow space between the meshes of the net only if there is firm contact with the vascular wall, where the neo-intima cells may subside in bridging from one thread to the adjacent one. This, of course, cannot happen at the orifice of a collateral branch and, thus, at that level the newly formed intimal cylinder must have a continuity solution. Nonetheless, even though not in contact with the wall, these threads undergo blood-stream-generated circumferential lining and increase their diameter, thus proportionally reducing the width of the meshes. The long-term evolution of these changes with potency of the collateral branch and the possible role of anti-aggregants and anticoagulants in preventing thrombus formation in this area is, of course, of interest and should be evaluated in long-term experiments.

In conclusion, of course the effectiveness of the procedure in arresting the aneurysm progression and preventing rupture and dissection without affecting the blood flow in the collateral branches must be proved clinically. However the theoretical considerations and the present experimental results are strongly in favor of the clinical potential of this technique. In particular, the reinforcement at the intimal layer provided by neo-intima formation and by the net prosthesis framework can be expected, on a theoretical basis [5, 6, 8, 9, 16, 17, 19, 22], to be extremely effective in preventing both dissection and rupture.

After completion of the experimental phase, early clinical trials may be encouraged by the extremely low invasiveness of the procedure, that may potentially and hopefully be used even for aortic arch substitution (Fig. 9). Moreover, the low invasiveness and the possibility of sequential, repeated applications implicit with this technique, may justify the prophylactic ascending aorta and arch reinforcement in Marfan’s patients in the early stage of their disease, which has recently been recommended using standard open technique [16]. The substantial normality of the inner aorta of these patients at an early age makes this experimental model consistently similar to the target clinical condition, so that the same favorable results can reasonably be expected. Moreover the conclusive understanding that a disarrangement of the elastin fibrils network is at the basis of aneurysm formation in Marfan aortic disease [23], might acknowledge the re-establishment of a uniform and regular network strengthening of the vascular wall with a net prosthesis as a logic, direct correction of the primary defect.

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References


