# Inducing Vascular Anastomosis for Vascular Tissue Transplantation and Vascular Regeneration: In Vitro Models and Factors

Jamal Jalili Shahri (MD)[1], Shirin Saberianpour (Ph.D)[1*]

[1]Vascular and Endovascular Surgery Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.

## ARTICLE INFO

## ABSTRACT

Anastomosis is a term which means a connection between two tubes or branched passages.Veins and arteries connect to transport blood in the body and this connection is natural anastomosis Whenever a blood vessel becomes blocked anastomosis is a backup pathway for blood flow. As the number of patients with chronic organ failure is increasing there is also a rapid increase in the demand for organ transplantation. As a result of a complicated mechanisms in different studies , activation of some factors including FLT1 (Fms Related Receptor Tyrosine Kinase 1), macrophages, fibroblast, hypoxia, platelet drive growth factor, fibrin-based tissue ,mature vessel networks ,VEGF( Vascular endothelial growth factor) and mechanical processes are been inducing factors for vascular anastomosis. Certainly, vascular anastomosis models are necessary for in vitro vascular anastomosis formation to cover vessels with perivascular cells in a microfluidic device or discover new surgery techniques. In this study, an attempt was made to collect effective factors in inducing vascular anastomosis.

## Introduction

All vertebrates need blood vessels for tissue homeostasis. Neoangiogenesis which means new vessel growth is an essential process in wound repair to overcome tissue ischemia (1). Neo-angiogenesis also has some undesirable effects, such as tumor expansion. Also, whenever neo-angiogenesis becomes nonproductive and fails to oxygenate ischemic tissues, the underlying disease progresses, such as: diabetic retinopathy. Anastomosis is a term which means a connection between two tubes or branched passages (2).

Veins and arteries connect to transport blood in the body and this connection is natural anastomosis Whenever a blood vessel becomes blocked anastomosis is a backup pathway for blood flow (3). As the number of patients with chronic organ failure is increasing there is also a rapid increase in the demand for organ transplantation(4).A critical problem in transplantation, including liver and kidney, is organ shortage (5).Creating transplantable organ/tissue grafts in Vito is a solution for this organ shortage (6).

In recent years researchers have worked to make transplantable bioengineered tissue grafts in vitro (7). Rapid blood perfusion is necessary in maintenance of implanted tissue grafts after

*Corresponding author: Shirin Saberianpour,
Vascular and Endovascular Surgery Research Center, Mashhad University of Medical Sciences,Mashhad, Iran.
E-mail: saberianpoursh@mums.ac.ir
Tel: 00985138047201

transplantation and this can be achieved by creating vascular anastomosis(8). In this study, an attempt was made to collect effective factors in inducing vascular anastomosis.

## Literature review
### Circulatory anastomoses

There are two approaches for creating vascular anastomosis. Circulatory anastomosis means natural anastomosis between many arteries; for example, the inferior epigastric artery and superior epigastric artery, or the anterior and / or posterior communicating arteries in the Circle of Willis (9).The circulatory anastomosis consisted of arterial and venous anastomosis. There are two types of arterial anastomosis: actual arterial anastomosis (e.g. palmar arch, plantar arch) and potential arterial anastomosis (e.g. coronary arteries and cortical branch of cerebral arteries)(9). Whenever large blood supply is not needed anastomoses can help regulate systemic blood flow by forming alternative routes around capillary beds (10,11).

### Necessity

In deceased donor transplantation cold ischemia time (CIT) has been cited as an important and independent risk factor for delayed graft function (DGF)(12). Graft survival and function is also poor in DGF. DGF causes long hospital stay and more resource use (13).

WIT is an interesting research area and studies about warm ischemia time (WIT) effects on DGF are few. In live donor transplantation long WITs reduces graft survival. WITs are two types : organ procurement time and vascular anastomosis time (AT)(14).Vascular anastomosis should be secure without thrombosis. Uncertain sutures cause bleeding and pseudoaneurysm formation. Antithrombotic failure causes early anastomosis occlusion and intimal thickening and anastomosis stenosis (15). Anastomosis site and method and suturing procedure all are important in vascular anastomosis formation (16).

### The difference between angiogenesis and anastomose

One of the fundamental processes in vertebrate developments is the formation of new blood vessels, which is of two types, vasculogenesis and angiogenesis(17). Angiogenesis is the main vessel forming process, and it typically involves new endothelial cells generating from earlier blood vessels (i.e., formed during vasculogenesis)(18).

It is still uncertain how blood vessel networks spread out and are controlled afterwards. In angiogenesis, new vessel sprouts join together to reach perfusion. This process is referred to as angiogenesis (19).

The matrix is where the vessels sprout into and generate perfused bridging connections. This device produces correct synopses of in vitro anastomosis to be utilized for studying angiogenesis and new drug screening approaches (20, 21).

### Vascular anastomosis in vitro models

For maximum accuracy, is necessary for in vitro vascular anastomosis formation to cover vessels with perivascular cells in a microfluidic device (22). Researchers observed that seeding HUVECs on both sides of gel scaffolds inhibits vascular formation. On the other hand, seeding HUVECs on only one side led to formation of vascular networks (23). Through testing a series of HUVEC/MSC ratios, it was found that vascular anastomosis can be induced by adding MSCs (24).

More investigations by live-cell imaging of green fluorescent protein-expressing HUVECs showed the development of vascular anastomosis with continuous lumens in the span of 8 to 10 days (22). VEGF concentrations were analyzed through computational simulation and the results showed the importance of local VEGF gradients in vascular formation (25). The addition of MSCs, however, was found to be crucial for anastomosis. Through this anastomosis model, a better understanding of the development of tissue-engineered grafts can be achieved, and progresses made in constructing large tissues by assembling multiple tissue-engineered constructs (26).

A microfluidic device was introduced by Jonathan W. Song that is capable of a precise reproduction of dynamics of vascular anastomosis (27). Vascular anastomosis takes place in the process of angiogenesis in which the connection of vascular sprouts leads to perfusion. The matrix is where the vessels sprout into and generate perfused bridging connections. This device produces correct synopses of in vitro anastomosis to be utilized for studying angiogenesis and new drug screening approaches (20).

In a research method introduced by Xiaolin Wang (2016), a whole microvascular network can be created whose connections with microfluidic channels produce negligible leakage. In this method, various stages of vascular development can be simulated consecutively: vasculogenesis, endothelial cell (EC) lining, sprouting angiogenesis, and anastomosis. When, through vasculogenesis, a capillary network was formed inside the tissue chamber, a single

layer of ECs covered the walls of the adjoining microfluidic channels. These channels will later transform into the low pressure output ("vein") and high-pressure input ("artery") conduits. The structure of the capillary network and its junctions with the microfluidic channels were strengthened through sprouting angiogenesis.

Sprouting angiogenesis is a process that advances the anastomosis of the vasculature in the tissue chamber. The proposed system can acute physiological vascular interconnection of several on-chip tissue constructs. These constructs can then be used for modelling diseases in drug screening procedures, making the system highly practical (28). In an in vitro study, Ju Hun Yeon et al (2012) used human umbilical vein endothelial cells (HUVECs) to generate and characterize perfusable capillary networks in microfluidic devices (MFDs). Here, sets of 3D tubular capillaries with diameters between 50–150 μm and lengths between 100–1600 μm can be reproduced. Connected blood vessels were generated by filling up the microfluidic devices with fibrin gel and let specific gel structures remain in bridge channels.

A layer of HUVECs was applied on the solidified gel walls on opposite ends of the patterned 3D fibrin gel. This procedure allows for high resolution microscopy of live cells and is not limited to the endothelial cell type, making it a highly practical approach in studying anastomosis, angiogenesis, and vascular biology (21, 29).

### *Different factor for inducing vascular anastomose without surgery*

Vascular anastomosis is the most important technical step required for the possibility of free tissue transfer, and mismatch of the donor and recipient vessel size is the most common surgical challenge. As recent research have described a Different factor for inducing vascular anastomose without surgery to resolve this challenge, the goal of this study was to assess these newly described microvascular anastomosis methods. You can see Different factor for inducing vascular anastomose without surgery in Table 1 and inducing vascular anastomosis by different factors for vascular tissue transplantation and vascular regeneration in figure 1.
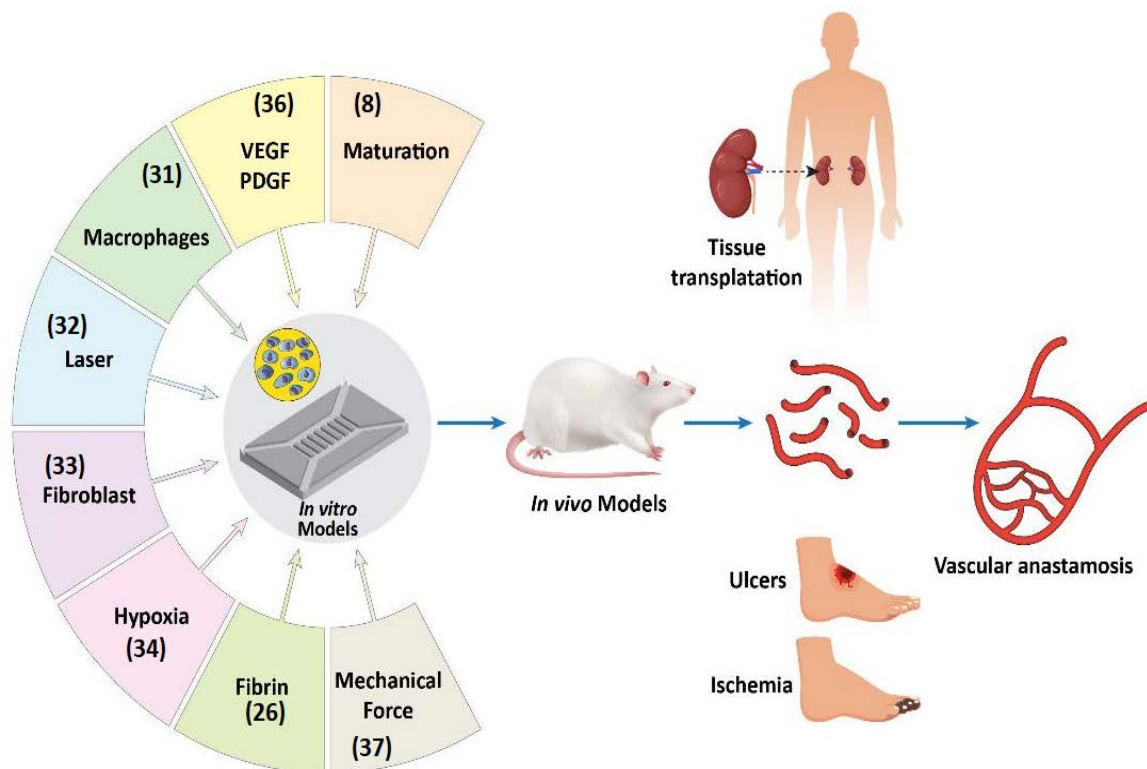


**Figure1:** Inducing vascular anastomosis by different factors for vascular tissue transplantation and vascular regeneration

### *FLT1 (Fms Related Receptor Tyrosine Kinase 1)*

Flt1 is responsible for regulating the dynamic characteristics of blood vessel sprout anastomosis, and ensuring of the connection site selection being a regulated process and not fully stochastic(30).

It has been demonstrated that the amount of VEGF receptor Flt1 is the selective regulatory factor of the connection site during the blood vessel network formation (31).

A large number of transient contacts have been observed to precede the formation of stable connections. Although their number is regulated by Flt1, these contacts do not exhibit bias towards Flt1 amounts at separate sites (32). This implies that transient contacts have an "exploratory" nature. However, lower amounts of Flt1, and possibly higher amounts of VEGF signaling, affect sites of anastomosis for target endothelial cells (32). As this bias is related to mFlt1 and unrelated to Flt1, it further demonstrates that a membrane-localized decoy receptor for VEGFA is responsible for regulating the target site selection in a cell-autonomous manner (33).

### Macrophages

In a number of diseases, pathologic angiogenesis is advanced by macrophages (34). This way, at adult sites of VEGF expression, pro-antigenic macrophages cells are created in the bone marrow (35). These cells are then recruited into growing tumors for furthering the vascularization, leading to their progression. The role of macrophages in some diseases alternates between constructive and injurious (36). In artery occlusion models, for instance, although macrophages exacerbate intra-aortic atherosclerosis, yet they can also further collateral growth, thus reducing the risk of ischemia (37). The macrophages in the retina (whether resident or recruited) have been observed to be involved in angiogenesis, both developmental and pathologic (38).

The contradictory role of macrophages hints at the existence of subpopulations, and, if distinguishable in function and molecular characteristics, the possibility of selecting between pro- and antiangiogenic types (39). Recently, a study further showed the existence of a subtype of monocytes in the blood of healthy adults that lacks any inflammatory profile and is similar in phonotype to the type of macrophage that contributes to tumor angiogenesis (40). These two types are similar in the expression of the 2 transmembrane proteins (necessary for angiogenesis), the angiopoietin receptor TIE2 and the multifunctional NRP1 protein, a receptor for specific class 3 Semaphorins and VEGF isoforms that are responsible for regulating intercellular adhesion (41). Before the production of monocyte-derived macrophages in the human embryo, there is a population of TIE2-expressing macrophages (TEMs) similar in antigens. It can be concluded that the cells have not been very well understood (42).

### Laser

Nine vascular anastomoses were carried out with lasers with a mean duration of 20 minutes (43). The duration of conventional anastomoses were 30 minutes (p less than 0.05). At the end of the experiment, all anastomoses were patent. In average, eight pulses with a duration of 2 to 4 seconds were applied in laser-assisted anastomosis (44). The results at the end of 13 weeks showed an average external diameter of 1.8 mm (+15%) for conventional anastomoses and 3.0 mm (+81%) in laser-assisted anastomoses (P less than 0.05)(45). The latter were all patent, functioned well, and showed no sign of stenosis, the fact that was observed in one out of five conventional anastomoses (46).

At the microanatomy level, the fibrosis caused by laser was negligible or nonexistent. This paved the way for regulated physiologic healing and normal growth. It was verified –via electron microscopy- that the arterial layers were re-integrated. It can be concluded that it is possible to implement a low-energy carbon dioxide laser for anastomosis of small growing vessels in clinical settings (47).

### Fibroblasts

Engineered implantable tissues with a thickness over 2–3 mm are dependent for survival on a convection of nutrients and waste products that facilitates transport. Researches attempted to create a network of vessels in vitro by creating a three-dimensional engineered vessel networks (48). The procedure began by a seven-day co-culture of endothelial cells (ECs) and fibroblasts in a fibrin gel, followed by formation of vessels through cord blood endothelial progenitor cell–derived ECs (EPC-ECs)(49).

High density fibroblasts were able to generate an interconnected tubular network faster than low density fibroblasts (four days compared to five to seven days)(26). On the other hand, when prevascularized tissues were implanted into immunodeficient mice, the ability of EPC-ECs and HUVECs in forming anastomoses with the host vasculature differed significantly. In the first day, vascular beds generated from EPC-ECs were observed to perfuse; however, HUVEC-derived vessels showed no sign of perfusion (48).

### Hypoxia

An evaluation of how hypoxia affects cellular proliferation at an artery anastomosis site was performed by surgery (ex vivo)(50). To prevent blood diffusing from the adventitial surface, the vasa vasorum is dissected at the beginning of the surgery (51). Arterial suturing can also reduce blood diffusion from the luminal side.

As could be predicted, the artery oxygen tension curves are flat and depressed at Day 0

measurements compared to control levels (50). But oxygen tension curves are observed to be further depressed at Day 7. This may indicate that oxygen is being consumed at the anastomosis site. Factors including VEGF, bFGF, PDGF etc. may be released as a result of hypoxia in the artery wall (52). These factors may be upregulated by the same hypoxia, which may lead to SMC migration and proliferation. After a series of events, artery wall hypoxia continues to incite cellular activity until the vessel is occluded secondary to IH (48,53).

### Platelet-derived growth factor BB induces functional vascular anastomoses in vivo

Endothelial cells and arterial smooth muscle cells are responsible for producing secreted PDGF-like protein and both PDGF transcripts, and for expressing receptors for PDGF muscle cells (21). The in vivo stimulating effect of PDGF has been observed in the chicken chorioallantoic membrane assay, in dermal repair under both ischemic and nonischemic conditions, and within the stroma of PDGF-BB-secreting tumors (21). It is unknown how PDGF affects in vivo microvascular endothelial cells in these systems (54). In vitro studies on angiogenesis have shown contradicting results; however, the direct stimulating effect of PDGF-BB on stimulating endothelial cells appears certain (55).

The BB homodimer has been shown to usually have a more powerful effect compared to the other dimeric PDGFs. It has been proposed that localized delivery of PDGF-BB has a precise direct effect on the angiogenic phenotype in endothelial cells as no sustained inflammatory response and granulation tissue are observed. It can be concluded that functional new blood vessels and anastomose severed vessels can be formed by PDGF-BB in vivo without surgery. It is further shown that a therapeutic modality for restoring ischemic tissue is possible via exogenous cytokine-induced vascular reconnection (21,56).

### Fibrin-Based Tissue

In tissue engineering, creating truly functional vascular networks that can provide for living body tissue is a highly complicated issue (57). The functional anastomosis can be highly accelerated if a tissue construct with networks of well-formed capillaries is prevascularized for implantation. In a prevascularization procedure of fibrin-based tissues with capillary networks, human umbilical vein endothelial cells (HUVECs) and fibroblasts were cocultured in fibrin gels (26). After one week, it was found that a prevascularized fibrin-based tissue with well-formed capillaries produces an earlier anastomosis with the host vasculature, and advances cellular activity in consistence with tissue remodeling (26). It may also be useful to employ prevascularization in designing larger 3D engineered tissues (26,58).

### Mature vessel networks in engineered tissue

Although, as mentioned above, in vitro prevascularization of engineered tissues accelerates anastomosis between the graft and host vasculatures, there have been instances of thrombosis following graft implantation (59). A study investigated the capability of in vitro vessel maturation in advancing vascular integration and graft perfusion, and in preventing instances of thrombosis in the transplantable grafts (60).

This study carried out a coculture of endothelial cells and fibroblasts on 3D scaffolds for a duration of one, seven, or 14 days and vasculatures were formed in varying stages of maturation (61). At the end of the 14th day, the interactions between graft and the host after implantation were investigated. It was found that anastomosis between the host graft and vessels cultured for 14 days was more advanced as their vessel networks had grown more complex (i.e., had elongated and better branched vessels etc.)(61).

The opposite was true for constructs with a shorter duration of culture; they exhibited inadequate vascularization and more thrombotic events (62). Also, in constructs in lower stages of vascular maturation, coagulation factors, von Willebrand factor (vWF), and tissue factor (TF) were expressed in higher levels (61,63). A pre-implantation engineered tissue featuring an already mature and complex vessel network will substantially enhance the strength and speed of perfusion (63). It has also been observed that engineered blood vessels in higher stages of maturation (more than one day before implantation) were able to effectively reduce the adhesion and accumulation of platelets in prevascularized grafts (64).

It can therefore be concluded that, if grafts are not prevascularized, their implantation may induce platelet activity and clotting cascade, leading to blood clot accumulation in the graft. In addition to graft failure, blood clotting can cause potentially fatal secondary thrombi in distal tissues (65). As a result of a complicated mechanism, activation of platelets through inefficient engineered vasculature produces a prothrombotic phenotype (66).

### VEGF

In vitro, vascular endothelial growth factor (VEGF) is a known endothelial cell-specific c mitogen. In vivo, it is the major mediator of angiogenesis (67). A correlation exists between the tissue edema resulting from burn and serum levels of

VEGF. An extensive distribution of VEGF mRNA and protein have been observed in normal rat tissues and organs, which supports the importance of VEGF in maintaining and controlling the vascular function (68). The amount of VEGF in the vein graft and arterial anastomosis shows a considerable increase 48 hours after arterial reconstruction via venous conduits (69).

In four weeks, the vascular VEGF expression returns to normal levels. However, it is still elevated in the adjoining arterial area. VEGF is still produced following arterial grafting and facilitates rET (70). This has a favorable effect on reaching optimal patency rates with autologous vein grafts .Ten days after surgery on rat femoral arteries, the production of VEGF is highly increased in sites of vascular anastomosis, as rat femoral arteries are the sites of VEGF-specific receptor flk-1 expression, and clearly upregulated ten days after surgical intervention (71).

### *Mechanical processes*

Vessel anastomosis can highly benefit from mechanical processes (72). In fact, when a tip cell neighbors an existing vessel, its filopodia projection can sense their microenvironment and attempt to connect to their filopodia or to other endothelial cells (73).

The VE-cadherins that exist in the filopodia tighten this connection. The tip cell moves forward towards the existing vessel and attaches to it. Next, the two lumina at this junction begin to gradually merge (74).

Mechanical factors can make further anastomoses even in more separated sprout networks. As an instance, when two tip cells come to direct contact, their exerted force is enough to produce a local deformation in the matrix and other tip cells may follow these deformation gradients (75). A tip cell can, therefore, sense its neighboring tip cells and move towards them. Still, the extent of this mechanism is relatively low (depending on the cell size)(76). In longer distances from a tip cell, the deformation of the tissue is not sufficient for guiding its neighboring cells (77).

There are other tissues in which mechanical processes are farther-reaching. An instance is the retinal tissue, where a layer of astrocytes guides and supports blood vessels from below (78). Here, the contact of the astrocytes network with endothelial cells above is mediated by filopodia as it guides the neo-vessels to restructure. It can be concluded that the astrocytes network can greatly advance the vessel anastomoses in the retina (79). Table 1 shows different factors for inducing vascular anastomose without surgery. Figure 1shows Inducing vascular anastomosis by different factors in in vitro, in vivo and clinical studies.

**Table 1:** Different factors for inducing vascular anastomose without surgery

| Factors | Mechanism | References |
|---|---|---|
| **FLT1 (Fms Relat-ed Receptor Ty-rosine Kinase 1)** | The amount of VEGF receptor Flt1 is the selective regulatory factor of the connection site during the blood vessel network formation | (30) |
| **Macrophages** | Macrophages inhibited remodeling of engineered vessels, infiltration of host vessels, and anastomosis with host vessels | (31) |
| **Laser** | Implement a low-energy carbon di-oxide laser for anastomosis of small growing vessels in clinical settings | (32) |
| **Fibroblasts** | High density fibroblasts were able to generate an interconnected tubular network faster than low density fi-broblasts | (33) |
| **Hypoxia** | Factors including VEGF, bFGF, PDGF etc. may be released as a re-sult of hypoxia in the artery wall.These factors may be upregu-lated by the same hypoxia, which may lead to SMC migration and proliferation. | (34) |
| **Platelet-derived Growth factor** | Functional new blood vessels and Anastomose severed vessels can be formed by PDGF in vivo without surgery by direct effect on the angi-ogenic phenotype in endothelial cells | (21) (35) |
| **Fibrin-Based Tis-sue** | Fibrin-Based Tissue can cause tissue construct with networks of well-formed capillaries | (26) |
| **Mature vessel networks in engi-neered tissue** | Blood vessels in higher stages of maturation are able to effectively re-duce the adhesion and accumulation of platelets in revascularization | (8) |
| **VEGF** | VEGF is a known endothelial cell-specific c mitogen. In vivo, it is the major mediator of angiogenesis | (36) |
| **Mechanical pro-cesses** | Mechanical factors can make further anastomoses even in more separated sprout networks. When two tip cells come to direct contact, their exerted force is enough to produce a local deformation in the matrix and other tip cells may follow these defor-mation gradients. | (37) |

### Non-suture methods of vascular anastomosis

The recovery of the anastomosis is affected by the inevitable vascular wall impairment induced by sutures(38). Other forms of incisions have become prevalent as well over time (38). The used materials place the non-suture techniques into five classifications comprising rings, clips, adhesives, stents, and laser welding. These crafts will ameliorate the trauma of anastomosis in comparison with suturing and also can be performed more quickly (38).

### Rings

While Payr was introducing an extraluminal magnesium prothesis7 around the 1900s, vascular anastomosing was also being instituted. In this approach, a ring was created to pass and evert the proximal vessel end onto it (39). Then, by pulling the proximal vessel end toward the dilated distal vessel, it was feasible to securely perform a circumferential ligature (39). Nonetheless, the perivascular inflammation and eventual occluding of the vessel was the outcome of magnesium absorption (40).

Every Teflon ring in paired anastomotic was utilized with 6 uniformly positioned pinholes and six pins interposed between each of them (41). Firstly, the arteries were enforced into the rings before their edges were being everted and fixated to the available pins. Then the approximation of the rings was performed. Lastly, every two rings were conjoined by two fixating sutures (41).

### Staples and clips

A stapler that was primarily assembled by Fischer to be employed in gastric resections was later used by a Hungarian surgeon named Hümér Hültl in the year 1908 (42). The crushing staple-forceps that was compiled to perform two twofold rows of U-shaped staples of steel wires bent into a B-shape sealing was constituted of a cogwheel, a gear rod, and a moving crankshaft. By using this device, both sides of the stomach were sealed together (43).

### Tubes and stents

An account initially articulated by Robert Abbe 52 in 1894 expressed the utilization of a tube or a stent for a vascular anastomosis. In his experiments conducted on animals, he stated the perpetually placed hourglass-shaped intraluminal glass tubes that were used as end-to-end anastomoses. The application on femoral arteries of the canine and the cat's aorta initially indicated desirable outcomes, nevertheless, occluding of the anastomoses occurred shortly after (44,45).

### Adhesives

Fibrin gules and cyanoacrylate glues are amongst the two classes of clinically used adhesives. The first glue comprises two components that replicate the last phase of blood coagulation. Fibrinogen, factor XIII, and plasma proteins are the main elements of the primary component; and the tertiary component contains thrombin, aprotinin, and calcium chloride. Matras et al initially introduced Fibrin Gule in 1977 to be applied to vascular anastomoses (46). The fibrin-sealed end-to-end carotid artery anastomoses performed on rats proved to be a risk-free and efficacious process given that the two 10/0 stay sutures were implemented indefinitely. The vascular anastomoses in dogs and rabbits that featured fibrin glue for end-to-side joins were primarily practiced by Gestring et al (38).

### Welding

Two vessel ends may be conjoined by another alternative process either by welding or lasers energy. As declared by Sigel and Acevedo in 1962, bipolar coagulation forceps may be employed in the operation of electrocautery in thermal welding. Another method outlined by Wintermantel engages geared approximator and hand-crafted wire loops. However, the thermally welded vascular anastomoses are not endorsed by clinical manifests as declared by the authors (47,48).

## Vascular Anastomosis during transplantation

Continuous sutures indicated more preferable results while being employed in anastomoses of small arteries in comparison with interrupted suture techniques (49). Arteries and veins of all sizes can benefit from the technically outlined continuous approach expressed in this article particularly in the rehabilitation of small vascular structures at the hepatic hilum during transplantation (50).Table 2 show Rapid Vascular Anastomosis during transplantation.

**Table2:** Rapid Vascular Anastomosis during transplantation

| Tissue | Technique | Model | Result | Reference |
|--------|-----------|-------|--------|-----------|
| **Hind-Limb** | Cuff Technique | (animal)Rat | Cuff technique provides a rapid and reliable surgical approach to rat hind-limb transplantation | (51) |
| **kidney** | DGF in a multivariable, binary logistic regression analysis | human | Anastomosis time may be an un-derappreciated but modifiable varia-ble in dictating use of hospital re-sources | (52) |

| uterine | end-to-side to the aorta and vena cava of the recipient animal | Ani-mal(mouse) | this was the first report of successful transplantation of the uterus with proven functionality in the mouse | (53) |
|---|---|---|---|---|
| small intesti-nal | formation of a "Cuff" | (Animal )rats | The SIS extracellular matrix served as a scaffold promoting host tissue in-growth | (54) |
| Liver | An absorbable vascular anastomosis device (AVAD) | (Animal )Pig | The success of the AVAD in the pig liver transplantation experiments and the feasibility of using an AVAD in organ transplantation | (55) |
| renal | surgical technique | low-weight children | The technical aspects of RT may re-duce the risk of compression of the iVC by the renal artery of the donor kidney | (56) |

## Conclusion

Vascular anastomosis is a process that actually completes the process of angiogenesis. Without vascular anastomosis, it will not be possible to complete the circulatory system for tissue function. In vascular surgery, vascular anastomosis is performed by invasive surgical methods. Recently, it is possible to induce this method by stimulating various factors. This approach will be very effective in organ transplant patients and the need for tissue regeneration such as chronic wounds due to weak immunity in these patients.

## Conflict of interest

The authors declare no conflicts of interest.

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