Which are the ideal donor and recipient vessels for a whole ovarian transplantation?

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Objective: To compare deep circumflex iliac (DCI) and deep inferior epigastric (DIE) pedicles as potential recipient vessels for a whole ovarian microvascular transplantation.
Design: Anatomical study.
Setting: Laboratory of anatomy, university center.
Patient(s): Ten fresh human female cadavers.
Intervention(s): Anatomical dissections, vascular injections, histologic analysis.
Main Outcome Measure(s): Morphological analysis of the gonadic, DCI, and DIE pedicles; diameter of the vessels at regular intervals along their entire length. Comparisons of the caliber values between receiving (DCI and DIE) and gonadic pedicles aiming to determine the optimal size match.
Result(s): We highlight a tortuous appearance of the gonadic artery. This morphology contrasted with the venous system that included two or three straight veins, one of them being wider than the others. The gonadic vessels converge into a wider artery and vein at 5 cm from the ovary. An optimal size match existed between gonadic and DCI arteries and veins sections, in 13 of 14 gonadic pedicles.
Conclusion(s): A safe microsurgical whole ovarian transplantation is feasible if the gonadic pedicle is harvested with a minimal length of 5 cm from the ovary. The DCI pedicle seems to have the best size match with the ovarian vessels to perform a reliable end-to-end microvascular anastomosis. (Fertil Steril® 2011;95:751–5. ©2011 by American Society for Reproductive Medicine.)

Key Words: Anatomy of the gonadic pedicle, anatomy of the deep circumflex iliac vessels, ovarian harvesting, transplantation, vascular anastomosis, fertility preservation

Cryopreservation of ovarian tissue is the only possibility of fertility preservation in patients requiring immediate chemotherapy or in patients without male partner (1–5). When the treatment has been completed and when the patient is in complete remission, the objective is to replant this ovarian tissue as an autologous graft in the subperitoneal layer of the pelvic cavity (orthotopic transplantation) or in a heterotopic site (forearm or abdominal wall). The initial phase of ovarian tissue ischemia occurring after transplantation is the limiting factor of this procedure, which unfortunately leads to the loss of two-thirds of the grafted follicles (6, 7). Reducing the long ischemic time between the reimplantation of the ovarian cortex and the spontaneous microscopic revascularization of the graft, therefore appears to be essential to maintain the viability of the follicles. Consequently, the best option to address this problem is to perform a whole ovarian transplantation in which the surgical restoration of the blood flow through arteries and veins of the gonadic pedicle provides an immediate revascularization of the transplant (8). The laparoscopic technique to harvest the ovary and its pedicle has been described by Jadoul et al. (9).

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The choice of the recipient pedicle has to fulfill several criteria (10).

- Easy surgical accessibility of the pedicle
- Feasible orthotopic transplantation into the pelvic cavity
- Optimal size match between the recipient pedicle and the gonadic vessels
- Possible postoperative ultrasound monitoring of the ovarian graft
- Easy puncture of the transplant for IVF

Optimal size match between the receiving pedicle and the gonadic vessels is one of the most prominent factor influencing the success rate of the transplantation. Several studies have shown that end-to-end anastomosis yields the highest patency rate of vascularized free grafts and flaps. Because specific blood flow dynamics take place in the small blood vessels, the risk of thrombosis is strongly reduced, when among all possible patterns of microvasclar

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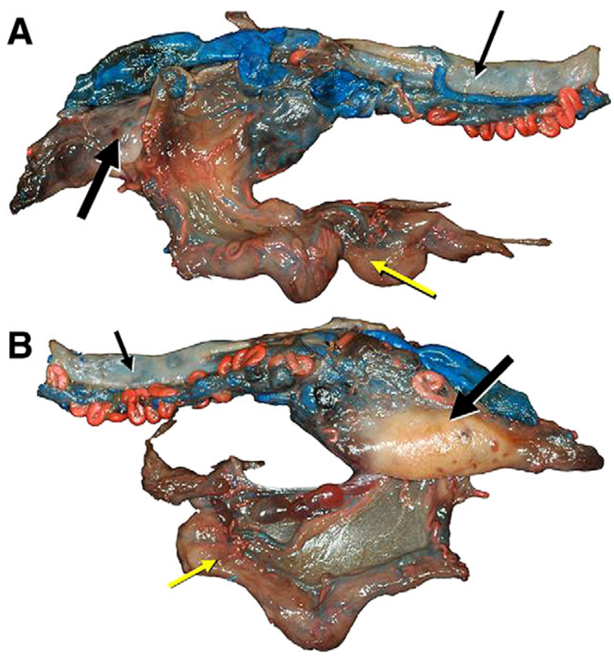
FIGURE 1

Right ovary (*thick arrow*) with the gonadic pedicle (*thin arrow*) and the fallopian tube (*yellow arrow*). (**A**) anterior view; (**B**) posterior view. Vascular injection with colored latex (artery *colored in red*, veins *colored in blue*). Gonadic artery had a sinuous aspect and its caliber is narrower than the gonadic veins.



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anastomoses, the vessels are sutured in an end-to-end fashion. Nevertheless, the technical feasibility of such a coaptation is restricted to specific anatomical conditions in which donor and recipient blood vessels exhibit comparable calibers, with a matching ratio not exceeding 1:1.5 (11).

According to some investigators, the deep inferior epigastric vessels (DIE) should be best suited for such an anatomosis (10). Based on our microsurgical experience with free tissue transfers in humans, we fear the opposite, that major size differences existing between the distal DIE and proximal gonadic vessels can sometimes result, intraoperatively, in difficult, mismatching, and unreliable anastomoses. In contrast, the deep circumflex iliac (DCI) pedicle seems to have nearest biometric features to the gonadic vessels during its entire course behind the inguinal ligament. The objectives of the present study were to compare the anatomical characteristics of DCI, DIE, and gonadic vessels at various points of their course and to emphasize the morphological guidelines for the donor and recipient vessels harvesting in view of whole ovary transplantation.

MATERIALS AND METHODS

The morphological characteristics of the gonadic, DIE, and DCI vessels were studied on 10 fresh human female cadavers. All were postmenopausal women. Vessels were exposed bilaterally by a transperitoneal approach and after detailed analysis of their respective courses, they were harvested in their entire length for histologic assessment.

In three cadavers, vascular injections were performed to emphasize arteries and veins. In one cadaver, corrosion casts of the gonadic vessels were obtained by injecting their lumens with a colored resin (polymethyl methacrylate, Altufix P10, Altulor, Paris, Défense 2, France). The prograde injection of the gonadic arteries was carried out with the liquid resin, colored in red, at their origin from the aorta. The gonadic veins were injected with blue resin, in a retrograde fashion, at their entrance in the left renal vein and the inferior vena cava. After solidification of the resin, corrosion of surrounding soft tissues took place in an acid bath. In two other cadavers, the gonadic vessels were injected with latex, which is more fluid than resin.

Untouched pedicles were harvested from seven bodies for precise biometrical measurements conducted on histologic specimens. Fourteen ovaries were harvested on their gonadic vascular pedicles, together with the homolateral DCI and DIE pedicles. Histologic analysis was then carried out on serial sections from these pedicles to measure the diameter of the vessels at regular intervals along their entire length. Standard hematoxylin and eosin and Weigert stains were used on the sections. Microscope slides were then digitized and studied by a picture analyzing program that calculates the theorical caliber of the vessels. The images were captured using the Leica Qwin, version 2.1, image analysis system (Leica Gmbh, Wetzlar, Germany). These caliber values were then compared between donor (DCI or DIE) and recipient (gonadic) pedicles to determine the optimal size match.

RESULTS

Gonadic Pedicle

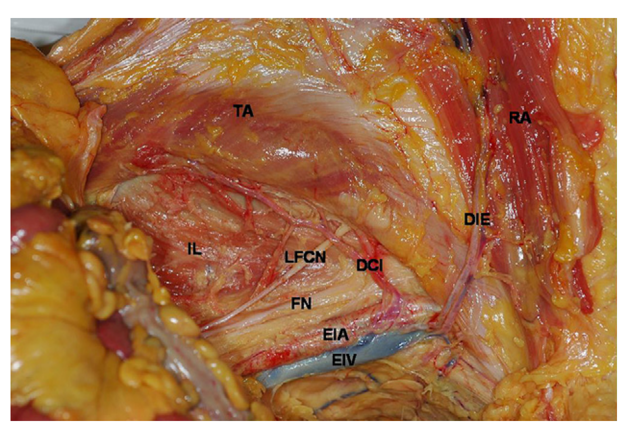
Vascular injections highlighted the very tortuous appearance of the ovarian artery. This arterial morphology contrasted with the organization of the proximal venous system, which always included two or three straight veins, one of them usually wider than the others (Fig. 1). The distal veins run around the ovary in a plexiform plexus.

Deep Circumflex Iliac Pedicle

The DCI pedicle arises from the lateral side of the terminal part of the external iliac vessels and heads for the anterior superior iliac spine. With its two veins, the artery runs under the fascia iliaca between the insertions of the transverse abdominis and the iliac muscles. Near the anterior superior iliac spine, the artery divides in two terminal branches: one goes toward the internal oblique muscle and

FIGURE 2

Left deep circumflex iliac (DCI) and left deep inferior epigastric (DIE) pedicles. Medial view of the left pelvis of a fresh human female cadaver. DCI and DIE pedicles arise from the external iliac vessels (EIA, EIV). The anatomical relationships of these pedicles are shown with the iliac (Il), transverse abdominis (TA), the rectus abdominis (RA) muscles and with the femoral (FN) and lateral femoral cutaneous (LFCN).



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the other supplies the iliac bone. In its course, the DCI pedicle crosses the femoral nerve and the cutaneous lateral nerve of the thigh (Fig. 2).

Deep Inferior Epigastric Pedicle

The DIE pedicle arises from the medial side of the termination of the external iliac vessels. It runs along the deep inguinal ring and continues its course upward behind the rectus abdominis muscle.

Histologic Study, Picture Analysis, and Quantitative Data

According to gross anatomy and vascular injection techniques, the gonadic artery has a highly tortuous appearance. This unique morphological characteristic gives the artery a false appearance of multiplicity on the stained histologic slides, as several sections of that vessel will occur on each sample under study. Therefore, interpretation of the arterial sections of the microscopic material has to be cautious and one has to refer to the anatomical data that only one ovarian artery usually exists in the gonadic pedicle.

Using our serial sections material we assessed the distance on the gonadic pedicle where the numerous gonadic vessels converged into a wider artery and vein. This critical point was located in all specimens at about 5 cm from the ovary (Fig. 3).

Thereafter, a mean vascular diameter (MVD) was calculated for the vessels of each pedicle (gonadic, DIE, DCI). This MVD allowed us to free ourselves from the tortuous appearance of the gonadic artery. In addition, it also permitted us to determine a mean caliber for the vessels constituting the different pedicles.

For each pedicle, all the biometric measurements were drawn in the form of a cloud of points. The diameter of each vessel was plotted on the y-axis and the distance from the origin of the vessel where the section was performed was then plotted on the x-axis. This presentation of these results allowed to us to correct some vascular diameters falsely increased by a tangential artifact of the cross section.

Individually, an optimal size match existed between gonadic and DCI arterial vessel sections in 13 of the 14 ovarian pedicles under study. Only in one case the best recipient site was the DIE pedicle. Six of the 14 gonadic pedicles did not have an artery with a diameter comparable with that of the DIE vessels. In addition, on two gonadic pedicles there was no vein with a diameter corresponding to the DIE veins. For each case the diameters of the DCI veins were closer to those of the gonadic vessels.

Finally, we determined the average vascular caliber of the gonadic donor vessels and the potential recipient pedicles (Table 1). For the gonadic pedicle, the artery had a consistent diameter of about 1 mm between 3 and 6 cm away from the ovary. The mean diameter of the DCI artery was 1.25 mm; this value attained 1.51 mm for the

FIGURE 3

Serial histologic sections of a gonadic pedicle at 1 (**A**), 2 (**B**), 3 (**C**), 4 (**D**), 5 (**E**), and 6 cm (**F**) from the ovary. Stain: HES-Weigert. Same magnification for the six sections. The critical point where the numerous vessels converge into a wider artery and vein is located at 5 cm from the ovary. On sections **A** and **F**, the principal arteries (A) and veins (V) are annotated (10x).

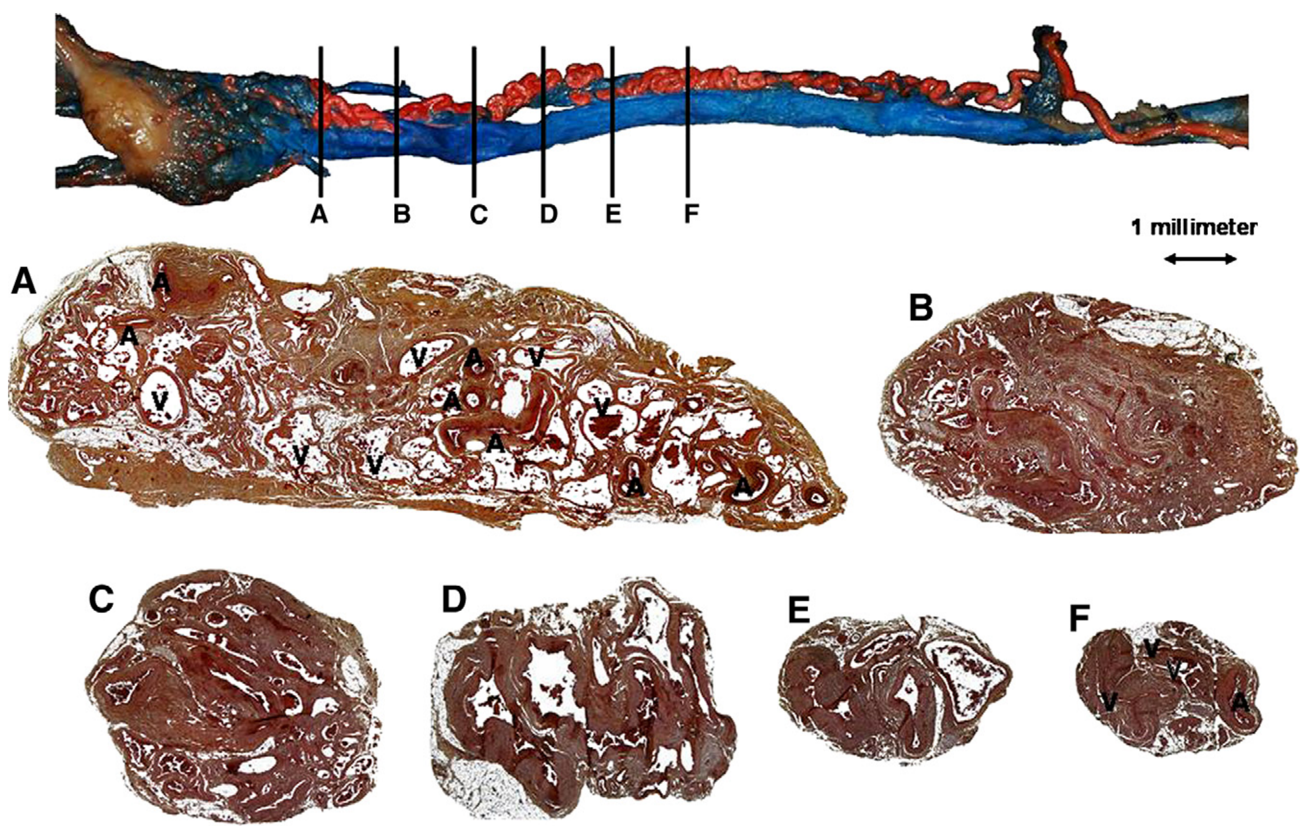

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TABLE 1

Average diameter of the gonadic, deep circumflex iliac, and deep inferior epigastric vessels.

Average diameter (in millimeters) of the deep circumflex iliac pedicle (SD)				
Artery	1.25 (0.10)			
Vein	1.18 (0.17)			
Average diameter (in millimeters) of the deep inferior epigastric pedicle at 5 cm from its origin on the external iliac vessels (SD)				
Artery	1.51 (0.17)			
Vein	1.31 (0.20)			
	Average diameter (in millimeters) of the gonadic pedicle (SD)			
	At 3 cm from the ovary	**At 4 cm from the ovary**	**At 5 cm from the ovary**	**At 6 cm from the ovary**
Artery	0.93 (0.22)	0.94 (0.21)	0.97 (0.20)	1.00 (0.19)
Vein	1.14 (0.31)	1.24 (0.16)	1.13 (0.26)	1.22 (0.32)

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DIE artery. The mean transverse section of the gonadic vein measured 1.20 mm, which is closely comparable with the DCI vein diameter at 1.18 mm. Furthermore, the DCI vessels were found to rotate easily in the upper pelvic inlet when dissected at least 5 cm from their origin on the iliac vessels.

DISCUSSION

Whole ovarian transplantation permits immediate revascularization of the transplant thus limiting the accelerated follicular loss due to ischemic injuries. According to published literature whole ovarian transplantation is generally limited to animal trials (12–14). Silber et al. (15) have reported the first successful pregnancy in humans after orthotopic whole ovarian transplantation between monozygotic twins.

Our morphological study demonstrates that a safe microsurgical whole ovarian transplantation is feasible if the gonadic pedicle is harvested at a minimal length of 5 cm from the ovary. At that point the pedicle contains at least one large artery and one dominant vein with both an average diameter of 1 mm. This is a landmark for the surgeon to consider when performing under laparoscopic approach the proximal retrograde dissection of the lombo-ovarian fold, which contains the donor gonadic vessels. Cutting the pedicle shorter than 5 cm from the ovary exposes the risk of finding a quite narrow artery surrounded by a plexus of very thin veins during additional in vitro dissection of the pedicle under microscope (9). This is a situation that may lead to a very uncomfortable and unreliable—if not impossible—microsurgical work.

From our observations the DCI pedicle seems to show the best size match for the ovarian vessels to perform a reliable end-to-end microvascular anastomosis. Furthermore, the rotation of the DCI pedicle in the pelvis should allow for an orthotopic ovarian transplantation. In fact, the optimal size match between the receiving pedicle and the gonadic vessels is one of the most important predicting factors in terms of success of the transplantation. Several studies have shown that end-to-end vascular anastomosis is the most reliable technique in revascularizing free tissue transfers and allografts. However, such an anastomosis can only be achieved by suturing vessels of identical or nearly similar calibers (ratio 1:1.5) (16). A sudden change of caliber may cause turbulence in the blood flow and predispose to platelet aggregation on the vascular walls surrounding the suture line with subsequent arterial or vein thrombosis, which unfortunately could lead to the failure of the transplantation. Below this ratio end-to-end anastomoses are reliable at 96%. Beyond this ratio, the donor versus recipient vessel discrepancy may be managed by microsurgical methods, such as oblique cut, fish mouth cut, or end-to-side anastomosis (11), to reach an adequate functional patency of the blood vessel connection and to reduce the risk of thrombosis (16). However, these intricate anastomoses have a higher rate of vascular complications. In animal models, ovarian transplantation carried out with an end-to-end anastomosis appears to be the best with a success rate higher than 60% (10). In their experiments, Bedaiwy and Falcone (10) also suggested that the inferior epigastric vessels were probably the most suitable heterotopic donor vessels, but their conclusions, drawn from a study performed on Merino sheep, cannot be transposed to humans. Classic anatomical studies in humans have shown that DIE vessels are subject to variations, that they do not have the same caliber along their entire course, and that their diameter gradually decreases, along their successive branchings supplying the peritoneum and the rectus sheath, until they finally enter the muscle.

We estimated a MVD for the gonadic, DCI, and DIE pedicles to have an objective idea of the morphological characteristics of their respective vessels. On the gonadic pedicle, between 3 and 6 cm upstream from the ovary, the gonadic artery had a constant diameter of about 1 mm. The ovarian artery shows thus a better size match with the DCI artery (MVD: 1.25 mm) than the DIE artery (MVD: 1.5mm). In contrast to the arterial system, two to three gonadic veins exist, with a prominent one showing an MVD ranging from 1.13 to 1.34 mm, which also best matched the MVD of the DCI veins (1.18 mm). Consequently, according to our data, DCI blood vessels should be harvested as the first choice pedicle to receive a whole ovarian graft. Nevertheless, although somewhat larger, the DIE pedicle remains an alternative donor site for recipient vessels if the harvest of the DCI pedicle fails or functionally delivers low blood flow vessels.

Furthermore, these conclusions about the ideal recipient pedicle for ovarian transplantation obviously have some limits that should be taken into consideration in the interpretation of our quantitative data. During the image analysis, the vascular adventitia was often damaged and we had to consider the external elastic lamina as the outer limit of the vessel. The cross sections of the vessels were not strictly transversal, especially as a result of the sinuous appearance of the ovarian artery, which could have falsely increased the MVD of the gonadic pedicle. Some biodynamic characteristics of donor and recipient vessels are probably underestimated on the cadaveric material because of the menopausal status, which probably reduces the size of the vessels.

Transplantation of an intact ovary with its vascular pedicle to the DCI vessels could have some advantages compared with other techniques. The recipient site is accessible and the surgical approach leaves a moderate cosmetic prejudice. An incision running 1 cm parallel to the inguinal fold is enough to reach the DCI vessels and free them on a distance of about 5 to 6 cm from their origin on the iliac vessels. Then, it is possible to carry out, outside of the abdomen, the microvascular time of the transplantation procedure. After revascularization of the ovary, the graft, rotating on its new pedicle of about 10 cm (5 + 5 cm), can be easily transposed just below the upper pelvic inlet, in an orthopic ovarian position, near the contralateral uterine tube to restore a functional infundibulo-ovarian unit. The approach to expose DEI vessels requires an inferior pararectal incision, which is much more harmful to the trophicity of the abdominal wall. The recipient site is accessible to ultrasonic monitoring and to oocyte retrieval.

In conclusion, whole ovarian transplantation may theoretically become a surgical reality. According to our data we have highlighted that such a procedure should meet two anatomical requirements: [1] the gonadic pedicle must be dissected at least 5 cm from the ovary, and [2] the recipient pedicle selection is first oriented on DCI vessels, although the DIE pedicle remains an alternative choice. Of course, because of the sample size, additional research must be done to confirm the suitability of the DCI pedicle for such an anatomosis.

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