Safety of Retrograde Flow of Internal Mammary Vein: Cadaveric Study and Anatomical Evidence

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Abstract

Background Additional second vessels may be required to handle multiple flaps used to add breast volume, boost blood flow for supercharging, or use salvage recipient vessels. In these situations, retrograde internal mammary vessel flow can be used although this causes doubts and concerns.

Patients and Methods Forty sides of the chests of 20 fresh cadavers with intact thoracic cages and internal mammary veins (IMV) were used in the study. IMV valve numbers and locations were checked, and the bifurcation was confirmed. A retrograde fluorescent angiography and a saline infusion test were followed to confirm flow direction.

Results Twenty-eight vessels were identified in 40 sides of the chest; of them, 45% had no valves. A mean 0.7 valves per chest side were identified; 23 (82.1%) of 28 valves were located above the second intercostal space (ICS). A mean 1.76 communicating veins were found between the IMV bifurcation. In all cadavers, a crossing vein connecting the left and right medial IMV was confirmed just below the xiphoid process. Fluorescent angiography and a saline infusion test proved that the retrograde flow was caudal through the bifurcated IMV to the communicating, intercostal, and crossing veins.

Conclusion The IMV valve was present in 55% of our subjects and located concentrically above the second ICS level. It is highly unlikely that the retrograde flow was disturbed because the retrograde anastomosis level was below the second ICS. Furthermore, the bifurcation, intercostal, and crossing veins across the xiphoid process enabled valve-less detour flow. Thus, retrograde IMV flow is considered safe.

The internal mammary artery (IMA) and vein (IMV) are among the most widely used recipient vessels for free autologous tissue-based breast reconstruction. In some cases, however, additional second vessels may be required to reconstruct a sizeable unilateral breast with multiple flaps, boost blood flow for supercharging purposes, or use the salvage recipient vessels when the antegrade flow of an internal mammary vessel is obstructed (►Fig. 1). In these situations, the retrograde direction of the internal mammary vessel can be used as a second recipient vessel.1–10 However, doubts and concerns persist about the safety of using this flow.11–13

The clinical application will increase if the principle of its safety of arterial input through retrograde IMA and venous outflow through retrograde IMV can be satisfied. First, concerns about the arterial system have been solved to some extent. The pressure of retrograde internal mammary artery (RIMA) was around 50 to 55 mm Hg, which was 77% of 70 mm Hg of the antegrade IMA (AIMA).7 Considering

Keywords
► internal mammary vein
► retrograde flow
► venous drainage
► valve

J Reconstr Microsurg 2020;36:316–324.

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that the pressure of the AIMA is equal to or higher than that of the systemic artery, the pressure of the RIMA is sufficient for flap perfusion. The actual RIMA pressure is not significantly different from that of the commonly used recipient artery at other sites such as the thoracodorsal artery.\textsuperscript{14} Furthermore, RIMA is also used for cardiac bypass surgery, in which the metabolic demand is high and muscle contraction is required.\textsuperscript{15–17} The flap currently used in breast reconstruction is a perforator-based adipocutaneous flap—such as the deep inferior epigastric artery perforator (DIEP) or profunda femoris artery perforator (PAP) flap—whose metabolic demands are lower than those of muscles or musculocutaneous flap, relieving worries without significant issues.

The precise rationale and principle of reverse flow in the retrograde IMV (RIMV) are unclear. It is necessary to overcome the valve to flow it backward and construct a collateral flow system to cope with it. First, controversy regarding the presence of valves in the IMV should be clarified, and it is necessary to confirm whether the reverse flow is sufficient through a collateral system.\textsuperscript{13,18} There are a couple of cadaveric studies on the presence of the valve. Al-Dhamin et al\textsuperscript{18} claimed that there is no valve in the IMV system and that flow through the RIMV would be safe. However, Mackey and Ramsey\textsuperscript{13} argued that valves are present and that the flow might be dangerous, thus showing different results.

To clarify the confusion of these conflicting results, here we investigated the incidence and location of the valve and assessed the principle of retrograde flow to confirm the retrograde flow.

**Patients and Methods**

Forty sides of the chest from 20 fresh cadavers with intact thoracic cage were used for this study. The anterior chest wall was separated from the thoracic cage to enable easy and accurate observation of the internal mammary vessel. Bilateral dissection of the internal mammary vessels on the anterior chest wall was conducted in a gross anatomy laboratory.

**Assessment of Valve Number and Location**

The anterior chest wall was turned inside out and approached from the inner side. The bilateral dissection was started from the first costal cartilage and descended to the xiphoid process level by the caudal direction. The IMV valve numbers and locations were checked (\textsuperscript{\textcopyright}Fig. 2). The valves from the right and left sides of the chest were identified. The bifurcation of the IMV was also assessed. From the first costal cartilage as the caudal direction, the bifurcation presence and level were confirmed. We also confirmed the presence of veins between two IMVs after the bifurcation and defined this vein as the communicating vein. Every measurement was performed by using digital vernier calipers (CD-15CP; Mistutoyo, Kawasaki, Japan).

![Fig. 2](image)
Assessment of IMV Retrograde Flow
An indocyanine green (ICG) fluorescent infusion study was performed to confirm the route of retrograde flow. ICG was injected in the second intercostal space (ICS) similar to the actual clinical situation. After puncture in the retrograde direction using an 18-gauge angio-catheter needle and antegrade direction was clamped with a mosquito, and 25 mg of ICG mixed with 20 cc of injection water was gently infused over 30 seconds. At the same time, a portable infrared camera (Moment-K; IAN C&S, Hanam, South Korea) was used to obtain images.

The second, third, and fourth ICS were dissected and opened and 20 cc of saline was infused again in the retrograde direction into the second ICS. The contralateral intercostal vein was checked to confirm the midline crossing flow (Fig. 3).

Assessment of Other Anatomical Data at the IMV
The height of each ICS and distance to the medial IMV from the lateral border of the sternum were identified. Descriptive statistics are expressed as means (±standard deviations). Student’s t-test was used to compare the right and left sides. p values < 0.05 were considered statistically significant. Data were analyzed using SPSS software version 21.0 (SPSS, Chicago, IL).

Results
The mean age of the cadavers used in the study (15 women and 5 men) was 83.7 years (range = 57–96 years). Of the 40 sides of the chest, 45% (n = 18) had 0 valves, 42.5% (n = 17) had 1, 5% (n = 2) had 2, and 7.5% (n = 3) had 3 (Table 1). Twenty-eight valves were identified in 40 sides of the chest; a mean 0.7 valves per side were identified. The locations where the valves were identified are summarized in Fig. 4: 57.1% (16/28) were on the left side, 42.9% (12/28) were on the right side; of them, 82.1% (23 of 28) were concentrated above the second ICS.

The bifurcation levels of the IMV are summarized in Fig. 5. On the right side, 45% were at the third ICS level, 30% were at the fourth ICS, 15% were at the second ICS, and 5% were at the first ICS. On the left side, 45% were at the third ICS, 30% were at the second ICS, 15% were at the first ICS, and 5% were at the fourth ICS. The frequency of bifurcation in both ICS was highest at the third ICS, and the left side was bifurcated sooner than the right side. However, 5% of vessels on both sides were not bifurcated. There were a mean 1.6 communicating veins on the right versus 1.95 on the left (average = 1.76, range = 1–4) (Fig. 6). In all cadavers, a crossing vein connecting the left and right medial IMV was confirmed directly at the level just below the xiphoid process (Fig. 7).

This finding was also revealed during ICG fluorescence angiography. Along with ICG flow, we were able to visualize the anatomy of the bifurcated IMV with the communicating, intercostal, and crossing veins (Fig. 8). When the saline infusion was performed in the retrograde direction, crossing flow across the midline was observed in the opposite intercostal vein (Fig. 9, Video 1).

Table 1 Number of valves by chest side

| Number of valves | Right side | Left side | Total |
|------------------|------------|-----------|-------|
| 0                | 11         | 7         | 18 (45%) |
| 1                | 7          | 10        | 17 (42.5%) |
| 2                | 1          | 3         | 4 (10%) |
| 3                | 1          | 0         | 1 (2.5%) |
| Total            | 20         | 20        | 40 (100%) |

The average heights of the ICS at the IMV are summarized in Table 2. The average height of the ICS at the IMV was 13.1 ± 5.0 mm. The widest space was the second ICS.

Fig. 3 Assessment of internal mammary vein retrograde flow. (A) Indocyanine green fluorescence infusion study and (B) saline infusion study.
Fig. 4 Location of the valve. Of our subjects, 82.1% (23 of 28) were concentrically located above the second ICS. Considering that retrograde anastomosis is performed mainly at or below the second ICS, the valve is less likely to be present at this level. ICS, intercostal space.

Fig. 5 Vessel bifurcation location. On the right side, the third intercostal space (ICS) was the most common, followed by the fourth ICS. On the left side, the third ICS was the most common, followed by the second ICS. ICS, intercostal space.
Fig. 6 Communicating vein between the internal mammary veins. There were a mean 1.76 communicating veins between the bifurcations.

Fig. 7 Crossing vein below the xiphoid process. In all cadavers, a crossing vein connecting the left and right medial internal mammary veins was confirmed directly at the level just below the xiphoid process.
(18.6 ± 4.0 mm), followed by the third ICS (14.9 ± 3.0 mm), first ICS (12.8 ± 4.1 mm), fourth ICS (11.3 ± 3.1 mm), and fifth ICS (7.8 ± 3.1 mm). In the fourth ICS, the right side was statistically significantly wider than the left side, but there were no significant differences in the other regions or the overall average.

The average distance from the IMV to the sternum is summarized in Table 3. The average distance from the IMV to the sternum was 8.0 ± 2.9 mm. That of the right side was 8.5 ± 2.9 mm, while that of the left side was 7.6 ± 2.9 mm. The right side was significantly distant from the sternum (p = 0.01). It also showed an increasing distance from the sternum.

Discussion

Use of the RIMV gives benefits when requiring a second recipient vein. It does not require additional dissection without changing the surgical field when the antegrade internal mammary vessel was used as the first recipient vein. The operation time can be shortened, reducing the surgeon’s physical and psychological fatigue. Furthermore, if the pedicle length is short such as when second flap is chosen as the PAP flap, transverse upper gracilis (TUG) flap, superior gluteal artery perforator (SGAP) flap, or lumbar artery perforator (LAP) flap, the use of an internal mammary vessel is more advantageous. It might not limit the choice of a second flap for stacked insetting.

The application of RIMV for breast reconstruction using a free transrectus abdominis muscle (TRAM) flap was first introduced by Li et al in 2002. With respect to DIEP, Kerr-Valentic et al used RIMV for the first time in 2009. After that several studies, including a cadaveric study, reported on the safety of RIMV flow since there was no valve in the IMV. ICG fluorescent angiography, duplex Doppler sonography, and pressure or velocity measurements have also been proposed to confirm sufficient retrograde flow for flap drainage. Based on this evidence, the use of RIMV is empowered in clinical practice.

However, the use of RIMV during DIEP flap breast reconstruction was not solely used for primary flap drainage but was mostly used for super drainage purposes as a second vein. It is unknown whether RIMV as the sole venous drainage was sufficient. For this reason, some researchers continue to voice uncertainty. According to Sugawara et al in 2015, it was difficult to guarantee a smooth outflow in 25% of RIMV cases. Mackey and Ramsey reported the existence of valves in the IMV, which is completely contrary to previously existing cadaveric results and raised the possibility of RIMV flow disturbances. These conflicting results from two studies confuse surgeons. On the other hand, clinical outcomes published by Stalder et al showed convincing evidence of the use of RIMV. While previous reports were based on the use of RIMV as the second vein for superdrainage of the DIEP flap, they used RIMV as the sole venous drainage while applying multiple flaps. They showed acceptable results with a 97.5% success rate of 41 flaps using only the retrograde limb. Moreover, Seth et al showed that while using the bipedicled DIEP flaps, abundant skin and soft tissue from the entire abdomen can result in improved breast shape.
The principle of how the RIMV previously have been misunderstood as no valves because found in 18 chest sides, 45% of the total 40 chests. It could each side, which was previously controversial. No IMV were as seen in the results, a mean 0.7 IMV valves were present on cadavers in particular are used to increase research accuracy. establish a basis for stability through our cadaveric study. Fresh remains unclear. For this reason, the authors attempted to demonstrate avalvular bypass drainage. Intraoperatively, the RIMV was transiently engorged after microanastomosis compared with the antegrade IMV (AIMV). This makes the surgeons uneasy and suspicious of RIMV flow. However, RIMV engorgement is naturally resolved after 5 to 10 minutes. According to previous reports, the average pressure of the RIMV was 8.7 ± 2.0 mm Hg, that of the AIMV was 5.3 ± 1.6 mm Hg, and the intraflap vein pressure of the DIEP was 17.7 ± 9.9 mm Hg. There was no statistically significant difference between RIMV and AIMV although the RIMV pressure tended to be higher than AIMV pressure and the venous pressure of the intraflap is much higher than the RIMV or AIMV pressure. Due to the pressure gradient, there is no problem with the flow direction from the flap to the RIMV or AIMV. However, immediately after vein anastomosis, the vein pressure of the intraflap did not exceed that of the RIMV, creating a temporary flow delay; if the inflow through the artery was sufficient, the venous outflow seemed to proceed smoothly.

Table 2 Height of intercostal space at the internal mammary vein

| Intercostal space | Right         | Left          | Total          | \(p\)-Value |
|-------------------|---------------|---------------|----------------|-------------|
| First             | 12.2 ± 2.8(8.3–17.0) | 13.5 ± 5.1(6.5–27.1) | 12.8 ± 4.1(6.5–27.1) | >0.05       |
| Second            | 19.0 ± 4.7(12.7–29.3) | 18.1 ± 3.4(11.5–23.2) | 18.6 ± 4.0(11.5–29.3) | >0.05       |
| Third             | 14.8 ± 3.3(8.9–22.8) | 15.0 ± 2.8(9.7–20.7) | 14.9 ± 3.0(8.9–22.8) | >0.05       |
| Fourth            | 12.1 ± 3.2(8.0–18.2) | 10.4 ± 2.9(6.0–17.8) | 11.3 ± 3.1(6.0–18.2) | 0.009\(^a\) |
| Fifth             | 8.1 ± 3.7(3.9–18.2)   | 7.5 ± 2.5(3.7–13.8)   | 7.8 ± 3.1(3.7–18.2)   | >0.05       |
| Average           | 13.3 ± 5.1(3.9–29.3)   | 12.9 ± 5.0(3.7–27.1)   | 13.1 ± 5.0(3.7–29.3)   | >0.05       |

\(^a\)\(p < 0.01\)

Note: Mean ± standard deviation (minimum–maximum); units, mm.
The authors obtained anatomical information through further assessments of the internal mammary vessels. In 2018, Lee et al. also published a cadaveric study of internal mammary vessels focusing on anatomical locations. The distance from the costochondral cartilage to the lateral IMV was used as a landmark to present the dissection parameter for recipient preparation for a beginner surgeon. However, if beginners cannot even accurately identify the costochondral junction from the outside, it may be challenging to establish a landmark; furthermore, the intercostal muscle and pleura are immediately adjacent to each other around this area—possibly resulting in pleural tearing. The results suggest that palpation of the sternum border may be a more straightforward method to determine whether to continue to approach the medial IMV from the sternum at a distance of approximately 5 to 9 mm from the lateral sternal border. It could also reduce the risk of pleural tearing. Also, the height of the second ICS is 18 to 19 mm, as shown in the results, which is usually sufficient for microanastomosis without rib cartilage resection. However, the third ICS space is narrower at 15 mm and narrows in the caudal direction, so the need for cartilage resection for microanastomosis may be greater at the level below the second ICS. The points that the position of the IMV bifurcation is mainly at the third ICS and that the left IMV bifurcates higher than the right IMV are similar to the results of Lee et al.

Inserting the bipedicled flaps or two flaps during surgery can lead to complications. To avoid this risk, the author performed total removal of the rib cartilage. There were two reasons for this decision. First, total cartilage removal allowed for a more comfortable microanastomosis by providing sufficient space for the four vessels without vascular kinking. Second, total cartilage removal can maximize pedicle length. The pedicle length of the PAP and TUG flaps, which are commonly used during stacked inset, is relatively shorter than that of the DIEP flap; therefore, it was necessary to prepare sufficient lengths of the recipient vessels.

The first limitation of this study is the pressure of the injected ICG or saline used to confirm the flow, that is, the pressure might not have been constant because we injected the solutions manually using an 18-gauge angio-catheter. We thought that gentle manual infusion would be similar and not significantly different from the intraflap pressure. The second study limitation is bias of the sample group, which included older cadavers of a single population (Asian). Third, all of the data were gathered from cadavers rather than live subjects. And fourth, the final quality outcome, such as fat necrosis and flap failure, could not be checked.

**Conclusion**

In this study, an IMV valve was present in 55% of subjects but absent in 45% of subjects. A mean 0.7 IMV valves were confirmed on each side of the chest and located concentrically above the second ICS level. It is highly unlikely that the retrograde flow was disturbed because the level of the retrograde anastomosis would be used below the second ICS. Furthermore, the bifurcation, intercostal, and crossing veins across the xiphoid process allow the valveless detour flow. In conclusion, our findings suggest the safety of retrograde IMV.

**Conflict of Interest**

None declared.

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| Internal mammary vein to sternum | Right | Left | Total | p-Value |
|----------------------------------|-------|------|-------|---------|
| First intercostal space          | 1.9 ± 3.9 (−5.9 to 8.9) | 2.9 ± 5.1 (−4.8 to 12.3) | 2.4 ± 4.5 (−5.9 to 12.3) | >0.05 |
| Second intercostal space         | 5.9 ± 2.8 (0.9–12.5)   | 5.6 ± 2.4 (2.2–10.1)    | 5.7 ± 2.6 (0.9–12.5)    | >0.05 |
| Third intercostal space          | 8.8 ± 3.1 (3.0–14.7)   | 7.3 ± 3.1 (2.3–14.3)    | 8.0 ± 3.2a (2.3–14.7)   | 0.033a |
| Fourth intercostal space         | 9.5 ± 2.3 (6.5–14.1)   | 8.5 ± 2.4 (3.3–13.6)    | 9.0 ± 2.4 (3.3–14.1)    | >0.05 |
| Fifth intercostal space          | 9.6 ± 1.8 (6.3–15.6)   | 8.9 ± 2.5 (4.4–13.5)    | 9.3 ± 2.2 (4.4–15.6)    | >0.05 |
| Average                          | 8.5 ± 2.9 (0.9–15.6)   | 7.6 ± 2.9 (2.2–14.3)    | 8.0 ± 2.9a (0.9–15.6)   | 0.01  |

*p < 0.05.

Note: Mean ± standard deviation (minimum–maximum); units, mm.
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