Meta-analysis of the effects of venous super-drainage in deep inferior epigastric artery perforator flaps for breast reconstruction

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Abstract
Introduction: Venous congestion is the most common vascular complication of the deep inferior epigastric artery perforator (DIEP) flaps. Adding a second venous drainage by anastomosing a flap vein and a recipient vein (super-drainage) is considered the solution of choice. Evidence to support this procedure, had not yet been confirmed by an analysis of the literature. We aimed to provide this evidence.

Materials and methods: We searched the literature (MedLine, Scopus, EMBASE, Cochrane Library, and Google Scholar), for studies discussing venous congestion and venous super-drainage in DIEP flap for breast reconstruction. Thirteen of the 35 articles compared results between one or two venous anastomoses. Meta-analysis was performed following PRISMA guidelines. Pooled risk ratio (RRs) for congestion, fat necrosis, partial necrosis, and total necrosis with corresponding 95% confidence intervals (CI) were calculated using a fixed-effect model with the Mantel–Haenszel method. The need to return to surgery (95% CI) was estimated with a random effect model using the DerSimonian and Liard method.

Results: We showed a statistically significant advantage of super-drainage to reduce the venous congestion of the flap (RR: 0.12, 95% CI: 0.04–0.34, p-value <.001), partial flap necrosis (RR: 0.50, 95% CI: 0.30–0.84, p-value .008), total flap necrosis (RR: 0.31, 95% CI: 0.11–0.85, p-value .023), and the need to take the patient back to surgery for perfusion-related complications (RR: 0.45, 95% CI: 0.21–0.99, p value .048).

Conclusions: Performing a second venous anastomosis between the SIEV and a recipient vein (venous superdrainage) reduces venous congestion and related complications in DIEP flaps for breast reconstruction.

1 INTRODUCTION

The Deep Inferior Epigastric artery Perforator (DIEP) flap, is considered the gold standard for autologous breast reconstruction (Bartlett et al., 2018). Flap failure is reported to occur in 1 to 5% of cases (Lie et al., 2013). However, the frequency of partial failures and their consequences is higher (Santanelli et al., 2015). The unsatisfactory results are frequently due to perfusion-related complications, developing in
FIGURE 1  Flow diagram that shows selection of articles

TABLE 1  Studies included in our meta-analysis

| Study       | Study type          | Flap 2vein | Recipient vein          | N. Cases | N. Controls | Mean OT cases (min) | Mean OT controls (min) | Difference in OT (min) |
|-------------|---------------------|------------|-------------------------|----------|-------------|---------------------|------------------------|------------------------|
| Ali, 2010   | Retrospective cohort| SIEV       | IMV                     | 21       | 11          | Na                  | Na                     | Na                     |
| Enajat, 2010| Retrospective cohort| SIEV       | Cephalic vein           | 291      | 273         | 383                 | 385                    | −2                     |
| Eom, 2011   | Retrospective cohort| SIEV       | LTV, branch of the TAV, IMVp | 45       | 108         | Na                  | Na                     | Na                     |
| Lee, 2012   | Retrospective cohort| SIEV       | Na                      | 18       | 68          | Na                  | Na                     | Na                     |
| Xin, 2012   | Retrospective cohort| SIEV       | TDV, LTV, ICV, SIEV, DIEV | 32       | 47          | 396                 | 366                    | + 30                   |
| Boutros, 2013| Retrospective cohort| SIEV       | IMVp, IMV               | 311      | 41          | Na                  | Na                     | Na                     |
| Ochoa, 2013 | Retrospective cohort| SIEV       | IMV                    | 87       | 639         | 314                 | 253                    | + 61                   |
| Al-Dhamin, 2014| Retrospective cohort| SIEV       | IMVr                  | 31       | 17          | Na                  | Na                     | Na                     |
| Santanelli, 2015| Retrospective cohort| SIEV     | SCV, TDV, IMV, SUV, LTV | 173      | 74          | Na                  | Na                     | Na                     |
| Ayestaray, 2016| Prospective cohort, randomized| SIEV | TAV                   | 23       | 29          | 510                 | 405                    | + 105                  |
| La Padula, 2016| Retrospective cohort| SIEV or second DIEV | IMVr                | 36       | 38          | Na                  | Na                     | Na                     |
| Unukovych, 2016| Retrospective cohort| SIEV       | Na                     | 211      | 272         | Na                  | Na                     | Na                     |
| Al Hindi, 2019 | Retrospective cohort| SIEV       | Cephalic vein          | 14       | 184         | 461                 | 356                    | + 105                  |

Note: "Cases": flaps with a second venous anastomosis. "Controls": flaps with a single venous anastomosis. In bold are the seven studies that were not analyzed in the previously published meta-analysis by Lee (Lee & Mun, 2017).

Abbreviations: AV, axillary vein; ICV, intercostal vein; IMV, internal mammary vein; IMVp, internal mammary vein perforator; IMVr, internal mammary vein retrograde branch; LTV, lateral thoracic vein; NA, not available; OT, operating time; SCV, scapular circumflex vein; SUV, subscapular vein; TAV, thoracoacromial vein; TDV, thoracodorsal vein.
up to 17% of DIEP flaps (Peeters et al., 2009). Venous congestion is the most common of the above-mentioned perfusion-related complications, with a reported incidence ranging from 2 to 20% (Kim et al., 2015; Sbitany et al., 2012) representing one of the main causes of fat necrosis, partial flap necrosis and, less frequently, complete necrosis of the flap (Santanelli et al., 2015). The etiology of venous congestion is multifactorial (Blondeel et al., 2000; Lundberg & Mark, 2006; Nahabedian et al., 2005; Rozen et al., 2009; Schaverien et al., 2010; Tran et al., 2007) with reversible and nonreversible causes.

When the causes of venous congestion are not reversible intraoperatively, treatment of the congestion itself is necessary and usually consists in increasing venous drainage of the flap by adding a second venous anastomosis between the flap and a recipient vein. The term flap supercharge or semantically more correctly, venous super-drainage is usually employed.

Several papers have been published highlighting the problem of DIEP’s venous congestion, and describing the surgical solutions available. Although there is no controversy regarding the use of flap super-drainage, which is the standard solution in case of venous congestion, evidence of the efficacy of this procedure on flap necrosis and vascular complications had not yet been reported.

To try to clarify the matter, we conducted a literature search statistically evaluating with a meta-analysis the relevant studies looking for evidence on the role of DIEP flap’s venous super-drainage in decreasing flap complications.

2 | MATERIALS AND METHODS

We performed a meta-analysis of the literature evaluating the role of a second venous anastomosis to prevent the complications of DIEP flap’s congestion. A literature search was conducted using MedLine, Scopus, EMBASE, Cochrane Library, and Google Scholar to identify and include all citations from 1994 to June 2019. To reduce inclusion bias, two of the Authors (VP and FG) performed, separately, the initial article search and selection with pertinent keywords (“Deep inferior epigastric perforator” or “DIEP” and “flap” (all fields) AND venous congestion (all fields) and (“additional anastomosis”) (Subheading) AND “superficial inferior epigastric vein” (All Fields) OR “SIEV” (all fields) AND “supercharging” OR “superdrain” OR “super-drainage”) (Figure 1).

Duplicated articles, isolated abstracts, case reports, correspondence, and letters were excluded and only full-text articles in
English regarding DIEP flaps and venous congestion were considered.

We followed the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA statement) (Moher et al., 2009).

We considered eligible the retrieved publications based on PICOS criteria (Patients, Interventions, Control/comparison, Outcomes, and Study Design), and analyzed by meta-analysis the incidence of perfusion-related complications: venous congestion, flap necrosis (total and partial), fat necrosis and need to take the patient back to surgery for perfusion-related complications. The most relevant data collected from the publications found were: first author, year of publication, number of patients and events, type of the second anastomosis and recipient vein, and operative time.

## 2.1 Statistical analysis

The Mantel–Haenszel test in R was used to calculate Pooled RRs and corresponding 95% confidence intervals (CI) for perfusion-related complications. The heterogeneity among studies was analyzed by using the $I^2$ test. We used a fixed-effects model for $I^2$ ranging from 0 to 30%; in the case of $I^2 > 30\%$, we applied a random effect model using the DerSimonian and Liard method.

For each test $p$ value ≤ 0.05 was set for significance.

## 3 RESULTS

After exclusion of nonrelevant papers, we identified 35 eligible articles and performed a qualitative evaluation following the guidelines of the Preferred Reporting Items for Systematic Reviews and meta-analysis (PRISMA statement) (Moher et al., 2009). Of these articles, 13 compared results between one or two venous anastomoses in DIEP flaps for breast reconstruction (Al Hindi et al., 2019; Al-Dhamin et al., 2014; Ali et al., 2010; Ayestaray et al., 2016; Boutros, 2013; Enajat et al., 2010; Eom et al., 2011; La Padula et al., 2016; Lee et al., 2013; Ochoa et al., 2013; Santanelli et al., 2015; Unukovych et al., 2016; Xin et al., 2012) and were included in our study. All the studies that we reviewed were retrospective, except the one by Ayestaray (Ayestaray et al., 2016), which is prospective and randomized.

Overall, our study analyzed 3,094 DIEPs, of which, 1,279 received a second venous anastomosis ("case group"); and 1,815 received only one venous anastomosis ("control group"). Venous congestion
occurred in 38 of 1,121 flaps, with an overall mean rate of 3.4%. The venous congestion rate in each study ranged from 0.9 to 36.5%. Regarding other perfusion-related complications, our literature review revealed 1.5% total flap loss (34/2278) (ranging from 0 to 9.6%), 6% partial flap loss (78/1294) (0 to 28.8%), 11.9% fat necrosis (217/1824) (7.2 to 34.6%), and 11.1% take back to surgery for perfusion-related complications (187/1678) (0.9 to 21.2%).

Of the 13 articles (Al Hindi et al., 2019; Al-Dhamin et al., 2014; Ali et al., 2010; Ayestaray et al., 2016; Boutros, 2013; Enajat et al., 2010; Eom et al., 2011; La Padula et al., 2016; Lee et al., 2013; Ochoa et al., 2013; Santanelli et al., 2015; Unukovych et al., 2016; Xin et al., 2012) included in our meta-analysis, 12 (Al Hindi et al., 2019; Al-Dhamin et al., 2014; Ali et al., 2010; Ayestaray et al., 2016; Boutros, 2013; Enajat et al., 2010; Eom et al., 2011; La Padula et al., 2016; Lee et al., 2013; Ochoa et al., 2013; Santanelli et al., 2015; Unukovych et al., 2016; Xin et al., 2012) reported the second anastomosis to have been performed between the SIEV and a recipient vein of the thorax, while in one study (La Padula et al., 2016) the second anastomosis was done using as flap vein the SIEV or a second DIEV, without additional information being provided. In all the articles included in our systematic review, performing an adjunctive anastomosis variably increased the operation time from no difference to 105 min (Table 1).

In more detail we found that anastomosing the SIEV of the flap with a recipient vein provided a statistically significant advantage in terms of venous congestion (RR: 0.12, 95% CI: 0.04–0.34, p-value <.001) (Figure 2) and to prevent flap necrosis both partial (RR: 0.50, 95% CI: 0.30–0.84, p-value .008) (Figure 3) and total (RR: 0.31, 95% CI: 0.11–0.85, p-value .023) (Figure 4). A second venous drainage showed a statistically significant advantage also regarding the need to take the patient back to surgery for perfusion-related complications (RR: 0.45, 95% CI: 0.21–0.99, p-value .048) (Figure 5). Conversely, the advantage of a second venous anastomosis was not significantly beneficial to prevent fat necrosis RR: 0.83, 95% CI: 0.63–1.10 reporting a p-value .19. (Figure 6).

4 | DISCUSSION

Although the DIEP flap is considered the gold standard for breast reconstruction, venous congestion can cause complete or partial flap failure and several other complications.

Our work, by reviewing the updated pertinent literature, aimed to provide evidence on the effect of super-drainage in terms of venous congestion and related complications. In case of intraoperative venous
congestion, the reversible causes can be identified and corrected. In particular, anastomotic failure requires resection of the anastomotic site, removal of any thrombus present, rinsing of the donor and recipient vessels with a heparinized solution (and, depending on the clinical situation, time since the beginning of occlusion and kind of flap, flap perfusion with thrombolytic agents), and vessels’ re-anastomosis. Vessel kinking can be solved by repositioning the entire pedicle of the flap by supporting it with a piece of fat or muscle, by stabilizing it with fibrin glue or by applying a stitch between the kinked vessel and the surrounding tissue to straighten its course. A mild to moderate torsion of a long pedicle can be solved simply by repositioning of the pedicle and therefore redistributing the torsion on its entire length. In more severe cases the anastomosis will need to be redone. If, in a large flap, the venous congestion is stable and only involves the distal portion of the flap, because of insufficient drainage despite effective outflow through the pedicle, resection of that area may be sufficient.

The second venous anastomosis, aimed to obtain a super-drainage of the flap, can be performed (a) between the deep venous system of the flap and a comitant vein of the recipient vessels (comitant DIEV-IMV) (La Padula et al., 2016; Marck et al., 1996), (b) between the deep venous system of the flap and a vein of the thorax (comitant DIEV-vein of thorax) (Fansa, 2019), (c) between the SIEV and the DIEV or to one of its side-branches (SIEV-DIEV) (Bartlett et al., 2018; Liu et al., 2007; Rohde & Keller, 2005; Sbitany et al., 2012; Xin et al., 2012), (d) Between SIEV and a vein of the thorax (Al Hindi et al., 2019; Al-Dhamin et al., 2014; Ali et al., 2010; Ayestaray et al., 2016; Boutros, 2013; Enajat et al., 2010; Eom et al., 2011; La Padula et al., 2016; Ochoa et al., 2013; Santanelli et al., 2015; Xin et al., 2012).

In physiologic conditions, the dominant venous drainage to the lower abdominal skin and fat is provided by the superficial venous system through the inferior epigastric vein (SIEV) (Enajat et al., 2010; Sbitany et al., 2012). All the papers included in our meta-analysis used the SIEV as a second vein of the flap to increase venous output. Table 1. The SIEV can be anastomosed, as said, to a vein of the deep venous system of the flap (intra-flap anastomosis) 1,5 or a vein of the patient’s chest (extra-flap anastomosis) (Eom et al., 2011).

Unfavorable anatomy of the venous system is considered among the most important, not-reversible, causes of venous congestion. Several studies (Kim et al., 2015; Rozen et al., 2009; Sbitany et al., 2012; Schaverien et al., 2008) attribute the clinical manifestations of venous congestion and the so-called perfusion-related complications to the lack of sufficient venous drainage from all areas of the flap (superficial, deep, ipsilateral, contralateral). Not all the factors related to the flap’s
venous anatomy can be modified by the surgeon. Therefore, accurate planning based on vascular anatomy is of utmost importance to prevent venous congestion of the flap. Computed tomographic angiography and magnetic resonance angiography permit to visualize the arterial system and, even more importantly, the venous connections between the deep and superficial systems, allowing to choose the most favorable perforators for optimal perfusion and drainage (Rozen et al., 2009; Schaverien et al., 2010). The ideal perforator will have a large caliber, a central position in the flap and numerous connections between the deep and superficial venous systems (Davis et al., 2019).

Once venous congestion occurs, and intraoperatively the reversible causes have been excluded, it is necessary to treat the venous congestion itself, by venous super-drainage.

One previously published meta-analysis, from Lee et al (Lee & Mun, 2017) showed that the use of super-drainage has a statistical advantage over venous congestion but only a trend toward a decreased risk of congestion-related complications. Further studies were, therefore, suggested. A detailed comparison with that previous meta-analysis (Lee & Mun, 2017), is presented in Table 2. Our analysis includes the six articles examined by Lee and seven additional ones, reporting on large groups of patients (Ochoa et al., 2013; Unukovych et al., 2016) and on a prospective randomized study (Ayestaray et al., 2016). (Table 1). Statistical methods were comparable but the larger amount of data, allowed us to achieve statistical evidence that the use of super-drainage, employing a second venous anastomosis between the SIEV and a recipient vein, reduces venous congestion, prevents partial and total flap necrosis, and the need to take the patient back to surgery. Unfortunately, the available data did not show a statistically significant advantage of a second venous anastomosis to prevent fat necrosis, a common complication (6 to 17.4%) in DIEP flaps.

However, from the results of our meta-analysis, there seems to be an advantage also in performing a second venous anastomosis in flaps without venous congestion. Therefore, the choice of performing routinely a second venous anastomosis should be considered.

A comparison between the super-drainage technique consisting in anastomosis of the SIEV to a recipient vein (the only one for which we have demonstrated a statistical advantage), and other techniques, such as DIEV to recipient vein, intermittent SIEV catheter drainage, or the application of leeches, was not feasible, based on the data available in the literature. The same problem exists regarding which vein the SIEV was anastomosed (e.g., retrograde IMV vs. cephalic turn-down).

A limitation of our study consists in the difficulty to achieve solid conclusions when working on mainly retrospective articles, none of

**FIGURE 6** Fat necrosis. Articles and related forest plots dealing with the complication. FN: number of flaps presenting Fat Necrosis.
which with an evidence level I or II (Table 1). However, our study follows the PRISMA guidelines (Moher et al., 2009), which warrant the quality of a meta-analysis.

Our study is the first to report statistically significant results on the subject of super-drainage. Our meta-analysis of the literature demonstrated the usefulness of venous superdrainage when performing DIEP flaps in postmastectomy breast reconstruction, an elective surgery burdened with relevant emotional implications for the patient. The use of an adjunctive venous anastomosis as a preventive measure could be considered.

| Articles included | Lee and Mun, 2017 | Pignatti et al, 2020 |
|-------------------|-------------------|----------------------|
|                   | Enajat, 2010      | All, 2010             |
|                   | Lee, 2012         | Enajat, 2010          |
|                   | Xin, 2012         | Eom, 2011             |
|                   | Santanelli, 2015  | Lee, 2012             |
|                   | Boutros, 2013     | Xin, 2012             |
|                   | Al-Dhamin, 2014   | Boutros, 2013          |

| Statistical analysis | Lee and Mun, 2017 | Pignatti et al, 2020 |
|----------------------|-------------------|----------------------|
| Pooled RRs and corresponding 95% confidence intervals (CI) for perfusion-related complications were calculated by the mantel–Haenszel test in RevMan 5.3. The heterogeneity among studies was evaluated with the I2 test. When I2 ranged from 0 to 30% a fixed-effects model was used. When the value of I2 exceeded 30%, a random effect model was used. | The mantel–Haenszel test in R was used to calculate pooled RRs and corresponding 95% confidence intervals (CI) for perfusion-related complications. The heterogeneity among studies was analyzed by using the I2 test. We used a fixed-effects model for I2 ranging from 0 to 30%; in the case of I2 > 30%, we applied a random effect model using the DerSimonian and Liard method. |

| N. of flaps. TOTAL | 1,376 | 3,094 |
|--------------------|-------|-------|
| N. of cases        | −842  | −1,279|
| N. of controls     | −534  | −1,815|
| Total flap loss    | RR: 0.97, 95% CI: 0.36–2.57; p = .94 | RR: 0.31, 95% CI: 0.11–0.85; p = .023 |
| Partial flap lost  | RR: 0.59, 95% CI: 0.18–1.94; p = .39 | RR: 0.50, 95% CI: 0.30–0.84; p = .008 |
| Fat necrosis       | RR: 0.87, 95% CI: 0.58–1.30; p = .49 | RR: 0.83, 95% CI: 0.63–1.10; p = .19 |
| Venous congestion  | RR: 0.06, 95% CI: 0.01–0.51; p = .01 | RR: 0.12, 95% CI: 0.04–0.34; p < .001 |

| Conclusion | Lee and Mun, 2017 | Pignatti et al, 2020 |
|------------|-------------------|----------------------|
| "The present review demonstrated that superdrainage using SIEV reduces the risk of flap congestion notably, while having little influence on flap survival. With regard to partial flap necrosis including partial flap loss and fat necrosis, general trends toward decreased risks were observed. However, statistical significance was not achieved and further studies would be needed." | "In conclusion, our meta-analysis shows, that venous super-drainage, that is, performing a second venous anastomosis between the superficial venous system and a recipient vein, provides a statistical advantage in terms of venous congestion and related complications in DIEP flaps for breast reconstruction." |

Note: Cases: flaps with a second venous anastomosis. Controls: only one venous anastomosis. In bold are the seven studies that were not analyzed in the previously published meta-analysis by Lee (Lee & Mun, 2017); "Cases": flaps with a second venous anastomosis. "Controls": flaps with a single venous anastomosis. Abbreviation: RR, risk ratio.

5 | CONCLUSIONS

In conclusion, our meta-analysis shows that venous super-drainage, that is, performing a second venous anastomosis between the superficial venous system and a recipient vein, provides a statistically significant advantage in terms of venous congestion and related complications in DIEP flaps for breast reconstruction.

CONFLICT OF INTEREST
The authors do not have any conflict of interest to disclose.
AUTHOR CONTRIBUTIONS
Marco Pignatti: Conceptualization, Data curation, Formal analysis, Writing—original draft, Writing—review and editing. Valentina Pinto: Conceptualization, Data curation, Formal analysis, Writing—original draft. Federico A. Giorgini: Conceptualization, Data curation. Maria Elisa Lozano Miralles: Conceptualization, Data curation. Salvatore D’Arpa: Conceptualization, Data curation. Writing—original draft, review and editing. Riccardo Cipriani: Conceptualization, Formal analysis, Writing—review and editing. Giorgio De Santis: Conceptualization, Formal analysis, Writing—original draft, Writing—review and editing.

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How to cite this article: Pignatti M, Pinto V, Giorgini FA, et al. Meta-analysis of the effects of venous super-drainage in deep inferior epigastric artery perforator flaps for breast reconstruction. Microsurgery. 2021;41:186–195. https://doi.org/10.1002/micr.30682