The Efficacy of the Surgical Delay Procedure in Pedicle TRAM Breast Reconstruction

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Abstract: Although experimental evidence suggests that the preliminary surgical delay procedure physiologically improves the circulation of the TRAM flap, there are no published controlled studies evaluating the clinical outcomes associated with this procedure. The purpose of this study was to evaluate the efficacy of the surgical flap delay versus no delay in consecutive patients having pedicle TRAM breast reconstruction.

This was a retrospective cohort study of breast cancer patients at the University of Michigan who had pedicle TRAM reconstruction between January 2004 and March 2008. Prior to September 2005, all patients had pedicle TRAM reconstruction without the delay procedure. Starting in September 2005, all patients had the delay procedure prior to TRAM flap reconstruction. Descriptive statistics were used to compare demographic data, comorbidities, and complication rates between the 2 cohorts. Regression analysis was used to determine the effects of the surgical delay procedure on the incidence of flap ischemia and major and minor complications while controlling for patient and treatment level factors.

Eighty-seven postmastectomy breast cancer patients had unipedicle TRAM flap reconstruction, in which 112 flaps were used to reconstruct breasts. The nondelay cohort consisted of 42 consecutive patients (51 flaps) and the delay cohort consisted of 45 consecutive patients (61 flaps). Of the patients without the surgical delay procedure 17.6% experienced at least one ischemic complication of the flap compared with 6.6% of those who were surgically delayed ($P = 0.082$). When controlling for patient and treatment level factors, the delay procedure was found to significantly decrease the incidence of flap ischemia (OR = 0.21, $P = 0.018$). In addition, there were no significant differences in the incidence of major or minor complication rates in the surgically delayed versus nondelayed groups ($P = 0.247$, $P = 0.486$, respectively). When patient and treatment level factors were taken into consideration, undergoing the delay procedure also did not increase the incidence of having a major or minor complication.

These data support the use of the preliminary surgical delay procedure to decrease ischemic complications of the flap in pedicle TRAM postmastectomy breast reconstruction.

Key Words: breast reconstruction, TRAM, delay, flap, ischemia, complications, postmastectomy reconstruction

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In recent years, many studies have demonstrated the aesthetic superiority of autogenous tissue over expander/implant techniques for postmastectomy breast reconstruction.[1–6]

Despite the growing use of perforator flaps in some centers, the pedicle TRAM flap remains a primary reconstructive option for many plastic surgeons. Like all flap-based options for breast reconstruction, the pedicle TRAM flap carries a potential risk of ischemia related tissue necrosis and flap loss. Although total flap losses are rare, pedicle TRAMs suffer partial flap loss or fat necrosis in 5% to 33% of reported retrospective reviews[7–9] and 14.5% to 16.2% of prospective analyses.[10,11] Technical modifications of the pedicle TRAM have mostly addressed improving flap perfusion to decrease the complications associated with tissue related ischemia. These include the upper abdominal TRAM flap,[12,13] the double pedicle TRAM flap,[14] the "supercharged" pedicle TRAM flap,[15] and the use of the preliminary surgical delay procedure.[10,16–20] The surgical delay procedure consists of ligation of the inferior epigastric vessels, days or weeks prior to breast reconstruction.

Experimental studies indicate that when the superficial and deep inferior epigastric systems are ligated in a surgical delay, choke vessels within the muscle dilate, with the venous system enlarging to allow for free flow toward the superior epigastric pedicle.[21] With delay, there is also an increase in the diameter and flow of the superior epigastric vessel artery.[22] Although experimental evidence suggests that surgical delays improve TRAM flap circulation, all clinical reports on this issue have been retrospective case series that are limited by the lack of comparative control groups. Consequently, the true clinical benefits of surgical delay for pedicle TRAM reconstruction remain uncertain. In addition, the extent to which patient and flap outcomes are affected by undergoing a surgical delay procedure is undetermined. Surgeons and patients need rigorous scientific evidence on which to base informed decisions regarding breast reconstruction procedures following mastectomy. The purpose of this cohort study was to evaluate the efficacy of the surgical flap delay in patients undergoing pedicle TRAM breast reconstruction.

METHODS

Study Population

The study evaluated breast cancer patients undergoing immediate or delayed, unilateral or bilateral unipedicle TRAM flap reconstruction from January 2004 to March 2008 by 2 surgeons at a single academic medical center. All patients reconstructed between January 2004 and August 2005 received pedicle TRAM reconstruction without the preliminary surgical delay procedure. Starting in September 2005, all patients received the delay procedure prior to the pedicle TRAM flap. All flaps were unipedicled and based on the ipsilateral rectus abdominis muscle. The delay procedure was carried out under general anesthesia in the outpatient setting. Both sets of deep and superficial inferior epigastric vessels were ligated, either with an open approach using a suprapubic skin incision or with an intraperitoneal laparoscopic approach. During the study period,

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there were no patients with bipedicle TRAM reconstruction or microvascular supercharging of the flap.

Data Collection

Patient demographic and clinical data were obtained through medical record abstraction. Demographic data collected included: patient age, height, weight, and comorbidities (diabetes, hypertension, hyperlipidemia, cardiovascular disease, vascular disease, thyroid disorders, lung disease, history of smoking within one year of breast reconstruction, and previous abdominal surgeries). Breast cancer-related data that were gathered included: use of preoperative or postoperative chemotherapy and radiation therapy. Procedural information collected included: laterality (unilateral vs. bilateral); timing of procedure (immediate vs. delayed); use of a surgical delay of the flap (delay vs. no delay); and number of days from the delay procedure to reconstruction.

Surgical complications were the major outcome of interest. A complication was defined as an adverse event occurring as a direct consequence of surgical reconstruction and requiring additional treatment beyond that normally associated with the reconstruction. Thus, a small suture sinus that required removal of a suture in an office setting was not considered a complication. The incidence of complications was evaluated in 2 ways: First, we assessed ischemia-related complications of the TRAM flap. Because patients with bilateral flaps could present with ischemic related complications to either flap and because patients with bilateral reconstruction had twice the chance of incurring an ischemic flap event, the unit of analysis was the flap, not the patient. An ischemia-related flap complication was defined as having one of the following: total flap loss (100% flap loss); partial flap loss (less than 100% flap loss) requiring operative intervention or salvage procedure; partial flap loss (less than 100%) treated nonoperatively with local wound care or dressing changes; or palpable fat necrosis. Next, we categorized all complications into either major or minor categories in which the unit of analysis was the patient. A major complication was defined as an adverse, surgery-related postoperative event that required readmission to the hospital or return to the operating room for an unexpected reason. Specifically, a major complication included any cardiovascular, thromboembolic, or pulmonary event; renal failure; cellulitis requiring intravenous antibiotics; infected mesh requiring removal; hernia or abdominal wall laxity requiring surgical repair; flap loss requiring revision or salvage procedure; and hematoma or seroma requiring surgical drainage. Minor complications included wound infection treated with oral antibiotics; seroma or hematoma not requiring operative drainage; mild abdominal wall laxity not requiring operative correction; venous congestion of the flap which resolved with topical nitrates; partial flap loss treated nonoperatively, and palpable fat necrosis.

Analysis

Descriptive statistics were used to compare demographic data, comorbidities, and the use of radiation or chemotherapy across the delay and nondelay cohorts. Pearson χ^2 analysis and Fisher exact test were used to compare the incidence of ischemia-related flap complications, as well as major and minor complication rates between the delay and nondelay groups.

Logistic regression was used to evaluate the association of the delay procedure with complications—ie, ischemic, major and minor complications—while controlling for potential confounding variables. Because we used the flap as the unit of analysis for ischemic flap complications, we used a generalized estimating equation to account for within-subject correlations while controlling for potential confounding variables. Due to limited sample size, we performed a backward stepwise regression for ischemic, major, and minor complications to determine which independent variables were not significant at the 0.05 level. The initial independent variables in our backward stepwise regression included (1) body mass index (BMI), (2) timing of surgery, (3) patient age, (4) history of preoperative or postoperative radiation, (5) history of preoperative or postoperative chemotherapy, and (6) use of the delay procedure. BMI was calculated using patients' preoperative heights and weights, using the formula, kg/m^2. We controlled for BMI as a continuous variable in the regression analyses because previous studies by our group and others have demonstrated a linear association between increasing BMI or obesity and higher complication rates in breast reconstruction.[10,23–25] Procedure timing (immediate or delayed) was included as a covariate due to its known association with complication rates, which our group has shown to be higher in the immediate setting.[10] Patient age was included in the analysis as a continuous variable because a previous analysis by our group found a higher rate of flap ischemia in older patients.[26] Radiation and chemotherapy were also included in the initial regression analysis because previous studies have shown higher complication rates in patients receiving these adjuvant therapies.[25,27] After performing backwards stepwise logistic regression, we limited our independent variables for all 3 regressions to age, BMI, and procedure type (delay or no delay). All analyses were performed with SPSS Version 16.0 (SPSS, Inc, Chicago, IL) statistical software package, and statistical significance was set at $P \leq 0.05$.

RESULTS

Eighty-seven patients underwent unipedicle TRAM flaps for postmastectomy breast reconstruction between January 2004 and March 2008, with 112 breasts reconstructed (62 unilateral and 25 bilateral) by 2 surgeons at the University of Michigan Medical Center. The nondelay cohort consisted of 42 consecutive patients through the end of August 2005 (51 flaps), whereas the delay cohort included 45 consecutive patients starting September 2005 (61 flaps). Of the 45 patients receiving the surgical delay procedure, 40 underwent deep inferior epigastric vessel ligation via an open approach, whereas 5 patients were delayed laparoscopically. Table 1 summarizes the study population by the 2 cohorts (nondelayed and delayed

TABLE 1. Study Population

	TRAM With Surgical Delay N = 45 Patients N (%)	TRAM Without Surgical Delay N = 42 Patients N (%)	*P*
Number of flaps	61	51	
Unilateral reconstruction	29	33	0.146*
Bilateral reconstruction	16	9	
Immediate reconstruction	19 (42)	26 (62)	0.066*
Delayed reconstruction	26 (58)	19 (45)	
Patient age, mean	47.4	47.5	0.964†
Patient BMI, mean	26.9	25.9	0.203†
Tobacco use within last 12 mo	5 (11)	2 (5)	0.435‡
HTN	6 (13)	5 (12)	0.841*
Asthma	6 (13)	2 (5)	0.268‡
Thyroid Dx	6 (13)	3 (7)	0.486‡
Dyslipidemia	3 (7)	5 (12)	0.475‡
Pre or postop radiation	16 (45)	20 (48)	0.254*
Pre or postop chemotherapy	26 (58)	20 (48)	0.343*

*Pearson χ^2.
†Independent sample *t* test.
‡Fisher exact test.

TABLE 2. Ischemic Complications of the Flap

	TRAM With Surgical Delay N = 61 Flaps N (%)	TRAM Without Surgical Delay N = 51 Flaps N (%)	*P*
Total flap loss	0	0	
Partial flap loss requiring operative debridement or salvage procedure	3/61 (4.9%)	5/51 (9.8%)	0.465*
Partial flap loss treated with local wound care	1/61 (1.6%)	1/51 (2.0%)	1.00
Palpable fat necrosis	0/61 (0%)	3/51 (5.9%)	0.091*
Incidence of at least one ischemic flap complication	4/61 (6.6%)	9/51 (17.6%)	0.082*

*Fisher exact test.

TABLE 3. Factors Associated With the Incidence of Ischemic Flap Complications in Pedicle TRAM Flaps

	Odds Ratio (CI)	*P*
Delay	0.21 (0.06, 0.76)	0.018
Age	1.18 (1.06, 1.30)	0.002
BMI	1.21 (1.02, 1.45)	0.031

flap patients). There were no significant differences in procedure timing, laterality, patient age, BMI, smoking history, comorbidities, radiation history, or chemotherapy history between the 2 groups. The average time from surgical delay to flap transfer was 39.93 days (range, 6–392 days, SD= 49.13 days).

Ischemic Flap Complications

Table 2 summarizes the incidence of ischemic flap complications by procedure type (flap with/without surgical delay). Of the patients who had a surgical delay of the pedicle TRAM flap, 6.6% had at least one ischemic complication compared with 17.6% of those without a flap delay. Without controlling for potential confounding variables, this difference was not statistically significant ($P = 0.082$). Similarly, there were no statistically significant group differences for particular types of ischemic events (ie, no differences in partial flap loss or fat necrosis rates). Table 3 describes results of the regression after controlling for potential confounding variables and within patient correlations, including procedure type (nondelayed and delayed flaps), patient age, and BMI. In this analysis, the use of preliminary surgical delay had a significant effect on ischemic flap complications (OR = 0.21, $P = 0.018$). These data suggest that performing the delay procedure significantly decreased the odds of having an ischemic flap event to approximately one-fifth that of the nonsurgically delayed group. Age was also found to significantly affect the incidence of flap ischemia, such that for every year increase in age, the odds of having an ischemic flap event rose by a factor of 1.18 (OR = 1.18, $P = 0.002$). Similarly, for every unit increase in BMI, the odds of having an ischemic flap event increased by a factor 1.21 (OR = 1.21, $P = 0.031$).

Major and Minor Complications

Table 4 summarizes the differences in major and minor complications in patients with and without the surgical delay procedure. There were no significant differences in major or minor complications between the delay and nondelay groups. Furthermore, when we analyzed individual complications using Pearson χ^2 analysis and Fisher exact test tests, we found no differences in the incidences of hernia, wound infection, delayed wound healing, hematoma, seroma, DVT, PE, pneumonia, or cardiac events between the delayed cohort and nondelayed cohort. Table 5 details the logistic regressions for both major and minor complications while controlling for procedure type (nondelayed and delayed flaps), patient age, and BMI. We found that the use of the delay procedure had no significant effects on the incidences of major or minor complications. Trends were observed in the regression for major complications associated with BMI. Higher patient BMI had an effect approaching significance on the incidence of major complications ($P = 0.067$), but not on the incidence of minor complications ($P = 0.227$).

TABLE 4. The Incidence of Major and Minor Complications

	TRAM With Surgical Delay N = 45 Patients N (%)	TRAM Without Surgical Delay N = 42 Patients N (%)	*P*
Major complications	10 (22)	14 (33)	0.247*
Minor complications	16 (36)	12 (29)	0.486*

*Pearson χ^2.

TABLE 5. Patient and Treatment Level Factors Affecting the Incidence of Major and Minor Complications in Patients

	Major Complications		Minor Complications	
	Odds Ratio (CI)	*P*	Odds Ratio (CI)	*P*
Delay	0.79 (0.31, 2.01)	0.627	2.0 (0.74, 5.39)	0.171
Age	1.01 (0.95, 1.07)	0.774	1.06 (0.98, 1.14)	0.144
BMI	1.15 (0.99, 1.33)	0.067	1.09 (0.94, 1.26)	0.277

DISCUSSION

Previous research has reported ischemic complications in 5% to 33% of pedicle TRAM flaps.[7–10] In this cohort study of surgically delayed versus nonsurgically delayed pedicle TRAM reconstructions, we found that performing the surgical delay procedure prior to definitive flap reconstruction produced a decrease in the incidence of flap ischemia from 17.6% to 6.6%. In fact, when patient and treatment level factors were controlled for, the odds of having an ischemic flap complication in patients undergoing the surgical delay procedure was approximately one-fifth that of the nonsurgically delayed cohort. Furthermore, women undergoing the delay procedure did not appear to be at increased risk for any other complications. Hartrampf et al[28] were the first to pose the question whether the surgical delay procedure should be routinely used in unipedicled TRAM flap reconstruction. We believe our data support the use of this approach for pedicle TRAM flaps.

The Efficacy of Flap Delay

Despite the vast amount of experimental evidence suggesting improved survivability and reliability of surgically delayed flaps,[18] the use of this procedure in TRAM flaps has usually been limited to high risk patients and to those with large tissue requirements.[19,22] Restifo et al studied 15 "high risk" patients undergoing the surgical delay procedure and found that the superior epigastric vessels of these patients underwent significant increases in diameter and flow by Doppler examination.[22] A clinical examination of vessel pressure by Codner et al noted that high risk patients had an increase in arterial pressure and a decrease in venous congestion of the TRAM

flap following surgical delay.[16] Ribuffo reported dilation of the superior epigastric vessels and a decrease in vessel resistance in high risk patients who underwent surgical delay.[20] In Erdmann and coworkers' series of 76 consecutive "high-risk" patients undergoing unipedicled TRAM flaps after delay procedures, he found a 6.6% partial flap necrosis rate.[10] Even with newer methods using laparoscopic/endoscopic techniques to ligate the deep inferior system, Restifo observed an increase in superior epigastric diameter and flow as demonstrated by Doppler in 8 high-risk patients. In all of these studies, risk factors for ischemic complications included a history of smoking, obesity, prior radiation therapy, a requirement for large volumes of transmidline tissue, or a combination of these factors. This was not the case for our surgically delayed cohort, in which all patients received the delay procedure regardless of risk profile and tissue requirements.

Because fat necrosis and acute partial flap loss can be unpredictable in unipedicled TRAM flaps, we recommend that the surgical delay procedure be performed in all patients presenting for this procedure. This notion is supported by Wang et al who performed a retrospective analysis of 107 consecutive patients undergoing delay procedures prior to unipedicled TRAM flap reconstruction and found that obese patients had the same rate of flap complications as normal weight patients.[24] Although one could interpret this finding as a justification for limiting delay procedures to obese patients (BMI >30), we observed a significant decrease in ischemic flap complications in surgically delayed patients, independent of BMI (Table 3).

Timing of Delay Procedures

The recommended time interval between TRAM flap delay and flap transfer remains controversial. Several studies advocate performing the delay procedure at least 2 weeks prior to definitive flap reconstruction.[22,29–34] Others recommend as little as 1 week.[31,35–39] Our patient population averaged 38.92 days between the delay procedure and TRAM flap reconstruction. Although we had a large standard deviation of 49.1 days, 80% of our patient population had the delay procedure between 12 to 44 days prior to TRAM flap reconstruction. There was one significant outlier who had TRAM flap reconstruction 392 days after the surgical delay procedure. Surgical delays at our institution are often performed at the time of sentinel node biopsy and TRAM flap reconstruction was often delayed in patients who required adjuvant radiation. This explains why the average time between delay and flap transfer was 40 days.

To determine the optimal time to wait between flap delay and breast reconstruction, we performed a separate regression analysis of the surgically delayed cohort and found no statistically significant effect of the delay time interval on the incidence of flap ischemia ($P = 0.963$). However, the improved outcomes of our surgically delayed cohort suggest that one should wait at least 2 weeks prior to tissue transfer. This is supported by the fact that vessel dilation, particularly choke vessel enlargement and angiogenesis, may occur as early as a few days postoperatively.[31,40–42] By day 14, proliferative clusters of cells coalesce into vascular cords which become functional vessels by day 21.[43]

Which Delay Technique "Works Best"?

Because a wide variety of delay techniques have been described in the literature, it is difficult to determine what constitutes an adequate delay procedure. This is a particularly vexing question: the vascular supply to the lower abdominal wall is extremely redundant with substantial blood flow coming from (among various sources) the superior epigastric, deep inferior epigastric, superficial inferior epigastric, and intercostal vessels. Some authors advocate incision of the skin periphery alone, whereas others ligate one or both of the deep and superficial inferior epigastric systems. Investigators have even recommended completely incising the skin island and elevating portions of the flap.[21,44–45] Advances in minimally invasive techniques have also introduced the laparoscopic delays in which the deep inferior epigastric vessels are ligated through an intraperitoneal approach. A selective arterial embolization technique has been described in which the deep inferior epigastric artery is embolized via a percutaneous catheter.[46] Further research is needed to determine precisely how many vessels must be occluded or ligated to obtain the benefits of the delay procedure.

At our institution, we limit the delay procedure to ligation of the deep and superficial inferior epigastric vessels. This is because factors thought to contribute to vascular failure in the pedicle TRAM include; (1) the limited number of musculocutaneous perforators in the periumbilical area to supply large amounts of blood to the abdominal tissue; (2) the random rather than axial pattern of blood supply in parts of the flap's skin island; (3) the presence of choke vessels which restrict the superior epigastric pedicle's perfusion of adjacent vascular territories;[22] and (4) reduction of flap perfusion pressure as a result of an increase in venous pressure during TRAM flap insetting.[47] With ligation of the deep and superficial epigastric systems, choke vessels within the muscle dilate, improving venous drainage into the superior epigastric pedicle.[18] With ligation of the deep and superficial epigastric vessels, there is also an increase in the diameter and flow of the superior epigastric vessel artery.[22]

Elevation of the flap's skin island is not carried out at the time of the delay due to the potential associated increase in post operative edema and seromas, thus making subsequent flap elevation more difficult. By limiting the extent of the delay operation, we also minimize recovery time. This minimalist approach has been supported by animal models of TRAM delay. In rats, Sano et al demonstrated that only a unilateral vascular delay of the ipsilateral deep or contralateral superficial system is needed to achieve the vascular benefits of the delay.[33]

Age and Ischemic Flap Complications

An interesting finding in this study was the association between increasing patient age and the greater likelihood of ischemic-related flap complications ($P = 0.002$, OR = 1.18). Our findings suggest that for every year of age increase, there was an increase in the incidence of ischemic flap complications by a factor of 1.18. Various factors may account for this finding: aging appears to have significant consequences for wound healing,[48] infection rates,[49] cardiac index, and renal function.[50] Although our previous research with the Michigan Breast Reconstruction Outcomes Study, a multisurgeon, multicenter prospective cohort study, did not note a statistically significant effect by age on major complication rates for either pedicle or free TRAM flaps,[10] we did not perform separate regressions that analyzed factors which solely affected flap outcomes. We found similar effects of age in a recent analysis of patients undergoing pedicle TRAM reconstruction at our institution between 1996 and 2006. In that analysis, patient age had a significant linear effect on the incidence of major complications and ischemic flap complications.[26] By contrast, other investigators have reported that patient age has little or no impact on complication rates. Girotto et al[51] found that the complication rate for older women (age 65 years or above) undergoing breast reconstruction did not differ significantly from that of younger patients (under 65 years). The Girotto study was limited by the small number of elderly patients (28 women, compared with 372 in the younger cohort). It is possible that in our single-center analysis, age was directly associated with a higher incidence of comorbidities.

Limitations

Our analysis should be interpreted in the context of some limitations. The limited numbers of participating patients may have left the study underpowered to detect significant differences for some of the outcomes assessed. Also, the single center study design may limit the generalizability of our findings to other sites or surgeons. Because of its retrospective cohort design, the study may have failed to control for all potential confounding variables. Although a randomized controlled trial (RCT) design would be more effective in controlling for confounders, it would also pose logistical and perhaps ethical challenges for both surgeons and patients. Based on our past experience with prospective studies, we find that providers and consumers are frequently reluctant to give up their rights to choose surgical procedures. Both parties often enter into this process with clear preferences for breast reconstruction procedures and may be unwilling to let randomization dictate their choices for reconstruction.

CONCLUSIONS

Despite the recent popularity of free tissue transfer for breast reconstruction, the pedicle TRAM flap remains a commonly used option. However, the pedicle TRAM flap is too frequently compromised by inadequate blood supply, resulting in partial or total flap loss. The preliminary delay procedure offers a simple, predictable method to significantly improve the reliability of pedicle TRAM flaps, without the technical and resource demands associated with more complex microsurgical flaps. We recommend that the surgical delay procedure be performed in all patients presenting for unipedicled TRAM reconstruction.

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