



# Should Sickle Cell Trait Be a Contraindication to Breast Reconstruction?—A Case Series Analysis

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J Reconstr Microsurg Open 2023;8:e51–e53.

## Abstract

**Background** While sickle cell disease has long been considered a contraindication to breast free flap reconstruction, there have been less definitive decisions about the impact of sickle cell trait on these procedures. We sought to analyze the patients with sickle cell trait who underwent free deep inferior epigastric perforator (DIEP) flap and pedicled latissimus dorsi (LD) flap at a single institution to determine the reconstructive outcomes.

**Methods** Patients with sickle cell trait who underwent breast free DIEP and pedicled LD reconstruction from 2007 to 2021 at a single institution by the lead surgeon were analyzed for demographics and surgical outcomes.

**Results** Four patients were identified as having sickle cell trait and having undergone a breast flap reconstruction. The average age of the patients was 54 years, median body mass index was 25, and past medical history was notable for one patient being a current smoker, and one patient having hypertension. Two patients received a unilateral free DIEP flap, one received a bilateral free DIEP flap, and one received a unilateral pedicled LD flap for a total of five flaps in four patients. Three of the patients received prior hormone therapy, one received prior radiation therapy, and one received prior chemotherapy. There were no instances of flap failure, vessel thrombosis, pulmonary embolism, or deep venous thrombosis. One patient experienced wound dehiscence.

**Conclusion** In this case series we present four patients with sickle cell trait who successfully underwent breast flap reconstruction without any instances of flap or systemic thrombosis. More work is needed to determine how to pre- and postoperatively optimize patients with sickle cell trait for favorable breast flap reconstruction outcomes.

## Keywords

- ▶ deep inferior epigastric perforator free flap
- ▶ latissimus dorsi flap
- ▶ DIEP
- ▶ sickle cell trait
- ▶ breast reconstruction
- ▶ autologous breast reconstruction

Sickle cell disease (SCD) is the most common genetic disease in the United States and affects 1 in 500 African Americans.<sup>1</sup> The presence of hemoglobin S (HbS) mutation promotes

hemoglobin beta chain polymerization under conditions of physiologic stress, such as dehydration, hypothermia, infection, and hypoxia, resulting in erythrocyte sickling. The

received  
December 2, 2022  
accepted after revision  
February 28, 2023

DOI <https://doi.org/10.1055/s-0043-1769752>.  
ISSN 2377-0813.

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**Table 1** Patient demographics

Patient	Age	BMI	PMH	Prior chemotherapy	Prior radiation therapy	Surgery type	ASA	Surgery duration (min)	Length of stay (d)
1	60	26	Former smoker	Yes	No	Unilateral DIEP flap	II	395	4
2	34	—	—	No	No	Unilateral DIEP flap	II	387	4
3	54	25	Current smoker	No	No	Bilateral DIEP flap	II	835	5
4	68	25	HTN	No	yes	Unilateral LD flap	II	353	2

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; DIEP, deep inferior epigastric perforator; HTN, hypertension; LD, latissimus dorsi; PMH, past medical history.

pathologic deformation and hyperviscosity of red blood cells are the principal drivers of small vessel occlusion and hypoxia characteristic of SCD. The release of inflammatory mediators and nitric oxide from ischemia, reperfusion injury, or both, further contribute to local tissue injury.<sup>1</sup> In addition to microvascular thrombosis, SCD patients experience higher rates of systemic thrombotic events such as pulmonary embolism and deep venous thrombosis (DVT) that further reduce life expectancy.<sup>2</sup>

Surgery poses many significant challenges for SCD patients and their care team, as the anesthetics used, immobility, relative hypothermia, and blood loss can all contribute to erythrocyte sickling.<sup>1</sup> The risk of microvascular and systemic thrombosis is accentuated in free flap-based breast reconstruction, in particular when the flap is detached from its native blood supply and not yet attached to its recipient vessels.<sup>3</sup> During this time of brief hypoxia, there is an increased risk of erythrocyte sickling which can lead to flap thrombosis and ultimately flap failure. As a result, SCD has been considered a relative contraindication to breast flap reconstruction due to the increased likelihood of flap and systemic thromboses. Less is known, however, with regards to the surgical risk posed by sickle cell trait (SCT), wherein up to 45% of hemoglobin is HbS.<sup>4</sup>

Although the risk is lower, the factors that promote vessel thrombosis and ultimately flap failure in SCD can also encourage erythrocyte sickling in SCT. To date, there has been no conclusive study to examine outcomes of free flap-based breast reconstruction in SCT patients, or whether SCT should be considered a relative contraindication to breast flap surgery. In this case series we present four patients with SCT who successfully underwent breast flap reconstruction.

## Methods

Patients with SCT who underwent breast flap reconstruction from 2007 to 2021 at a single cancer center by the lead surgeon were analyzed for demographics and surgical outcomes.

## Results

Four patients were identified as having SCT and having undergone a breast flap reconstruction. The average patient

age was 54 years and median body mass index was 25. Two patients received a unilateral free deep inferior epigastric perforator (DIEP) flap, one received a bilateral free DIEP flap, and one received a unilateral latissimus dorsi flap. A total of five flaps were identified. Three of the patients received prior hormone therapy, one received prior radiation therapy, and one received prior chemotherapy. Additional demographics and surgery descriptions are included in **Table 1**.

Among the four patients, there were no instances of flap failure, vessel thrombosis, DVT, or systemic venous thromboembolism. One patient experienced wound dehiscence and hernia, and another patient had fat necrosis (**Table 2**).

## Discussion

SCT and disease have been associated with thrombogenesis in part due to higher levels of procoagulant factors such as D-dimers, thrombin-antithrombin complexes, and monocyte levels.<sup>2</sup> Despite the procoagulant nature of SCT during times of stress, such as surgery, these patients did not experience any instances of flap thrombosis, flap failure, or systemic thromboembolism.

While some case studies performed on SCT patients argue that the genetic disease should be considered a relative contraindication similar to smoking (Mehta et al), others argue that the risks of ischemia and hypothermia can be localized to the flap itself and that SCT does not represent a systemic contraindication.<sup>2,5</sup> McAnney et al performed a bilateral DIEP flap on a patient with SCD and had a unilateral flap failure due to thrombosis postoperatively. They argued that flap hypothermia when cooling the left flap during harvest was the cause for failure in the context of the patient's SCT. The contralateral flap was not complicated by thrombotic sickling arguing against a system condition such as SCT as the principal cause. McAnney et al concluded that SCT was not a systemic contraindication for breast reconstruction.<sup>2</sup>

While there are no clear guidelines for surgical management of patients with SCT, prior case studies have presented strategies to reduce ischemia, hypothermia, and the risk of thrombosis. Optimized measures to prevent complications in SCT patients taken in other studies include doubling the dose of low molecular weight heparin after surgery (Young-

**Table 2** Patient outcomes

Patient	Flap	Complications	Flap failure	Vessel thrombosis	Systemic VTE	Additional surgeries
1	Unilateral DIEP flap	None	No	No	No	Revision
2	Unilateral DIEP flap	None	No	No	No	None
3	Left DIEP flap	Wound dehiscence	No	No	No	Revision
	Right DIEP flap	None	No	No	No	None
4	Unilateral LD flap	Fat necrosis	No	No	No	None

Abbreviations: DIEP, deep inferior epigastric perforator; LD, latissimus dorsi; VTE, venous thromboembolism.

Afat et al<sup>6</sup>), exchange transfusion to keep the HbS level lower than 25%<sup>4,6</sup> application of active heating to prevent hypothermia,<sup>7</sup> supplemental oxygen, aspirin, verapamil, nitroglycerin paste, phosphodiesterase inhibitors,<sup>7</sup> hypotonic fluids, and the use of a pedicled flap versus free flap when HbS is greater than 30%.<sup>5</sup> However, there is no consensus as to whether these measures should be universally adopted by all surgeons. Future studies regarding preoperative optimization of HbS content through the use of medications such as voxelator (hemoglobin polymerization inhibitor)<sup>8</sup> and hydroxyurea (increased production of fetal hemoglobin)<sup>9</sup> could also prove fruitful.

The patients in our case series presented with additional risk factors for thrombosis, including a history of smoking ( $n = 2$ ), hypertension ( $n = 1$ ), and a history of prior hormone therapy ( $n = 3$ ). Despite multiple risk factors, all four patients underwent successful microvascular free flap transfer or pedicled flap transfer without any thrombotic complications, indicating that such procedures may be considered feasible options for breast reconstruction in patients with SCT.

Limitations to the present study include a very small cohort size and a single surgeon's results, thus larger sample sizes will be needed. Further work to systematically evaluate the role of preoperative medical optimization, length of ischemia time, and exposure of flaps to low temperature will be needed to fully characterize the risk posed by SCT.

## Conclusion

SCT did not present an increased risk of flap failure, flap thrombosis, DVT, or systemic venous thrombosis in our case series of four patients undergoing breast flap reconstruction. More work is needed to determine how to pre- and postop-

eratively optimize patients with SCT for favorable breast flap reconstruction outcomes.

## Funding

This study was funded by NIH/NCI Fox Chase Cancer Center Support Grant P30CA006927.

## Conflict of Interest

None declared.

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