



GUIDELINES

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Letters

Does Previous Head and Neck Irradiation Increase Vascular Complications in Free Autologous Reconstruction?

Sir:

We read with interest the recent article "Free Flap Reconstruction in the Head and Neck Region following Radiotherapy: A Cohort Study Identifying Negative Outcome Predictors."¹ This is an important article because there are still contradicting data regarding microsurgical complications associated with previous radiotherapy. The topic is also of general interest outside the plastic surgery community because there is an increasing population of cancer survivors for whom the long-term side effects of radiotherapy have to be considered. In fact, a growing body of clinical evidence

has recently shown that radiotherapy is an independent risk factor for cardiovascular disease (i.e., myocardial infarction and stroke) at previously irradiated sites. This is further supported by molecular evidence that radiotherapy clearly exerts a detrimental effect on blood vessels, especially the endothelium.²

However, in the context of microvascular surgery, we lack a more detailed description of vascular complications related to radiotherapy. A relationship between previous chest wall irradiation and different vascular complications during free flap surgery was recently clearly shown in 1026 free flaps by Fosnot et al.,³ but this finding did not affect the free flap failure rates. The association shown by Fosnot et al., between radiotherapy and perioperative vascular complications, would be interesting to study in the cohort presented by Bourget et al., where the radiotherapy dose is higher (median, 64.5). Both studies concluded that radiotherapy is not associated with increased free flap failure rates. However, this could be explained by the fact that even relatively large clinical cohorts suffer with regard to statistical power as a result of low free flap failure rates, because it is difficult to detect an association with a limited sample size. In an attempt to overcome this, we presented a review of the literature where free flap outcome had been described in relation to previous radiotherapy. No association had been found between previous radiotherapy and complete free flap failure in any of the single studies, but a significant relationship between previous radiotherapy and free flap failure was clearly seen when all of the material was analyzed together ($p < 0.0019$; odds ratio, 1.72; 95 percent confidence interval, 1.22 to 2.44).⁴

There are several studies, outside the microsurgical field, that have been able to show that radiotherapy is associated with a prothrombotic response where the radiotherapy dose seems to be of importance.^{1,5} Fosnot et al. described that their results may be explained by endothelial dysfunction and prothrombotic characteristics seen in irradiated recipient veins, previously presented by us and others.⁶ Our group has over the past few years been studying radiation-induced gene expression in head and neck recipient arteries and veins and found an inflammatory and prothrombotic response even years after radiotherapy exposure.^{6,7} We believe that vascular complication is a more sensitive endpoint, compared with free flap failure, when radiotherapy shall be studied as a risk factor for microvascular surgery. Clinical studies on radiotherapy-related thrombosis during microsurgery in both arteries and veins may also contribute to increased general knowledge about radiation-induced vasculopathy, an area recently pointed out as an important field for future research in cancer survivors.¹

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REFERENCES

1. Bourget A, Chang JT, Wu DB, Chang CJ, Wei FC. Free flap reconstruction in the head and neck region following radiotherapy: A cohort study identifying negative outcome predictors. *Plast Reconstr Surg*. 2011;127:1901–1908.
2. Altena R, Perik PJ, van Veldhuisen DJ, de Vries EG, Gietema JA. Cardiovascular toxicity caused by cancer treatment: Strategies for early detection. *Lancet Oncol*. 2009;10:391–399.
3. Fosnot J, Fischer JP, Smartt JM Jr, et al. Does previous chest wall irradiation increase vascular complications in free autologous breast reconstruction? *Plast Reconstr Surg*. 2011;127:496–504.
4. Halle M, Bodin I, Tornvall P, Wickman M, Farnebo F, Arnander C. Timing of radiotherapy in head and neck free flap reconstruction: A study of postoperative complications. *J Plast Reconstr Aesthet Surg*. 2009;62:889–895.
5. Waksman R. Late thrombosis after radiation: Sitting on a time bomb. *Circulation*. 1999;100:780–782.
6. Halle M, Ekström M, Farnebo F, Tornvall P. Endothelial activation with prothrombotic response in irradiated microvascular recipient veins. *J Plast Reconstr Aesthet Surg*. 2010;63:1910–1916.
7. Halle M, Gabrielsen A, Paulsson-Berne G, et al. Sustained inflammation due to nuclear factor-kappa B activation in irradiated human arteries. *J Am Coll Cardiol*. 2010;55:1227–1236.

Reply: Does Previous Head and Neck Irradiation Increase Vascular Complications in Free Autologous Reconstruction?

Sir:

There are a number of points raised in the letter by Halle et al. First and foremost, the present study¹ should not be interpreted as indicating that the risk of complications is higher in the previously irradiated patient, as in this study there was no comparison with the nonirradiated patient. Rather, the study concerned negative outcome predictors in irradiated patients that can potentially be modified. The most significant of these was infection, with others such as flap size being beyond the control of the reconstructive surgeon.

However, there are other issues raised by Halle et al. that are important. There is the paradox that with lower flap failure rates in all forms of reconstruction, the use of flap failure as an endpoint is becoming less informative. Trends in outcomes analysis are therefore shifting from hard endpoints such as flap failure to slightly more subjective areas such as validated scoring systems. This is not to be criticized, as these in fact may be more informative than outcomes such as flap failure per se (e.g., the use of the Enneking scoring system in post-traumatic open tibial reconstruction).²

However, one must not choose a scoring system or endpoint that is more sensitive if it has no functional

relevance or influence on significant outcomes. The suggestion by Halle et al. to use vascular complications to increase the sensitivity of studies on preoperative radiotherapy is perhaps not a meaningful outcome in its own right. As pointed out by Fosnot et al., despite the significant differences found in their study on previously irradiated and nonirradiated free flap breast reconstructions in terms of vascular complications, this did not impact on meaningful overall outcomes.³ Rather, they conclude that it allows the surgeon to be prepared for a more challenging dissection and anastomosis.

Another approach to increase the sensitivity of studies is to combine multiple cohorts. This has been demonstrated to good effect in the study by Halle et al. on increased flap failure rates in preoperative radiotherapy in head and neck reconstruction.⁴ However, as they correctly point out, combining multiple cohort studies may increase power but also increases the risk of confounding variables (e.g., different surgical teams, techniques, postoperative regimens, and radiotherapy protocols). Failure rates in the subgroups analyzed ranged widely, from 0 to 17 percent. The quality of a meta-analysis depends critically on the quality of the data included. Therefore, the debate continues regarding the influence of radiotherapy on flap failure rates.

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REFERENCES

1. Bourget A, Chang JT, Wu DB, Chang CJ, Wei FC. Free flap reconstruction in the head and neck region following radiotherapy: A cohort study identifying negative outcome predictors. *Plast Reconstr Surg*. 2011;127:1901–1908.
2. Naique SB, Pearse M, Nanchahal J. Management of severe open tibial fractures: The need for combined orthopaedic and plastic surgical treatment in specialist centres. *J Bone Joint Surg Br*. 2006;88:351–357.
3. Fosnot J, Fischer JP, Smartt J Jr, et al. Does previous chest wall irradiation increase vascular complications in free autologous breast reconstruction? *Plast Reconstr Surg*. 2011;127:496–504.
4. Halle M, Bodin I, Tornvall P, Wickman M, Farnebo F, Arnander C. Timing of radiotherapy in head and neck free flap reconstruction: A study of postoperative complications. *J Plast Reconstr Aesthet Surg*. 2009;62:889–895.

Venous Thromboembolism following Microsurgical Breast Reconstruction: An Objective Analysis in 225 Consecutive Patients Using Low-Molecular-Weight Heparin Prophylaxis

Sir:

We read with interest the article on venous thromboembolism following microsurgical breast reconstruction and the use of low-molecular-weight heparin prophylaxis.¹ Postoperative deep vein thrombosis