

Safe Perioperative Tamoxifen Use in Autologous Breast Free Flap Reconstruction: Systematic Review and Meta-Analysis



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BACKGROUND

Tamoxifen's use in breast cancer has been an ongoing and integral part of perioperative therapy for women diagnosed with hormone-receptor-positive, early-stage breast cancer. Given that a large population of breast cancer patients will undergo mastectomy followed by autologous free flap breast reconstruction, it is critical to understand the effects of tamoxifen use on free flap survival. In the current body of literature there have been several conflicting reports leaving providers with more questions than answers regarding this challenging clinical circumstance.

OBJECTIVE

We aim to perform a systematic appraisal of the literature to determine if perioperative tamoxifen increases the risk of flap complications in autologous breast free flap reconstruction patients.

METHODS

A systematic literature search was performed using: Pubmed, EMBASE, Cochrane Central, Web of Science, EBSCO host, Clinicaltrials.gov, and TRIP databases from their inception to April 2021. Articles analyzing the impact of perioperative tamoxifen in autologous breast free flap patients were included. The outcomes assessed were total flap loss, overall flap complications, thrombotic flap complications, and systemic venous thromboembolism (VTE). Pooled estimates and relative risk were calculated using a random effects model.

RESULTS

Figure 1: Forest plot of pooled RR for the outcome of thrombotic flap complications. There is no significant heterogeneity ($\chi^2 = 8.19$, $I^2 = 39\%$, $p = 0.15$)

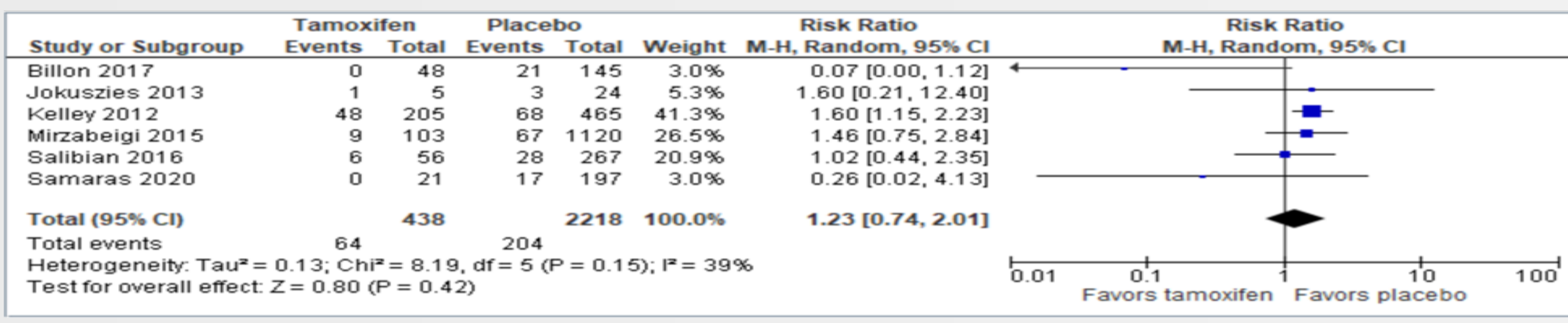


Figure 2: Forest plot of pooled RR for the outcome of total flap loss. There is no significant heterogeneity. ($\chi^2 = 8.17$, $I^2 = 39\%$, $p = 0.15$)

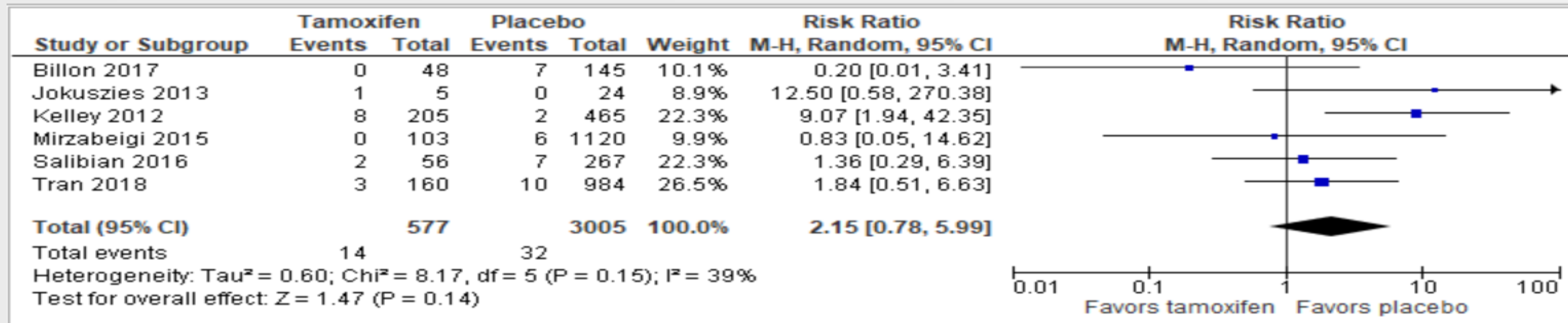


Figure 3: Forest plot of pooled RR for the outcome of overall flap complications. There is significant heterogeneity. ($\chi^2 = 27.81$, $I^2 = 78\%$, $p = 0.0001$)

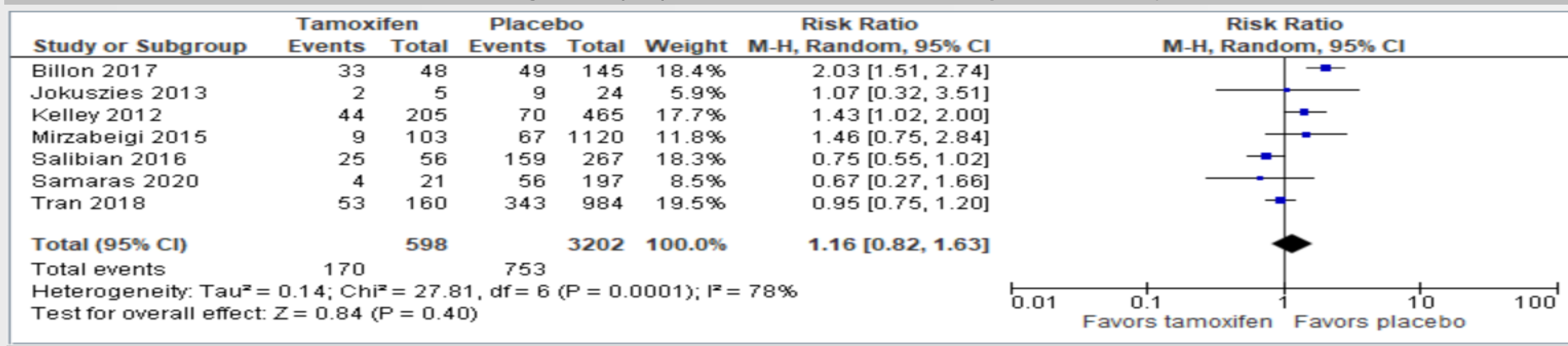


Figure 4: Forest plot of pooled RR for the outcome of systemic VTE. There is no significant heterogeneity. ($\chi^2 = 0.84$, $I^2 = 0\%$, $p = 0.93$)

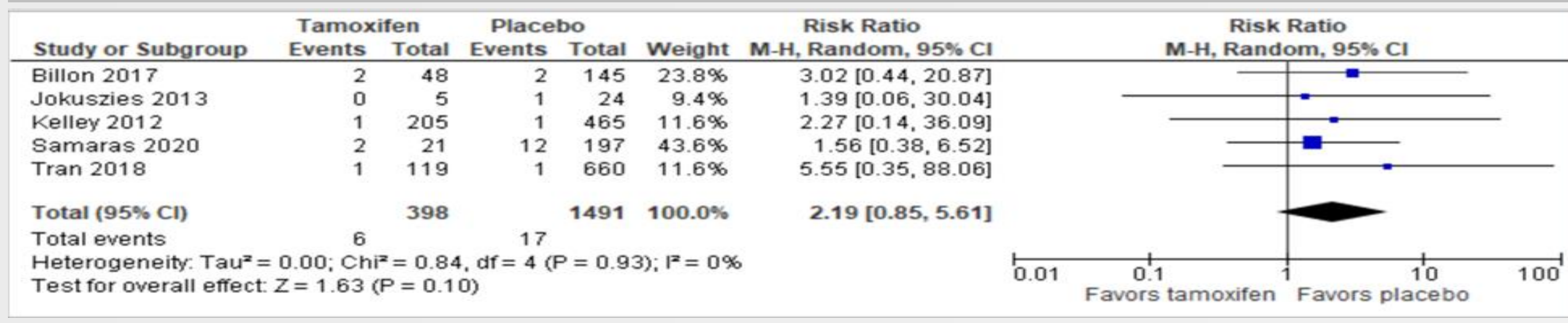
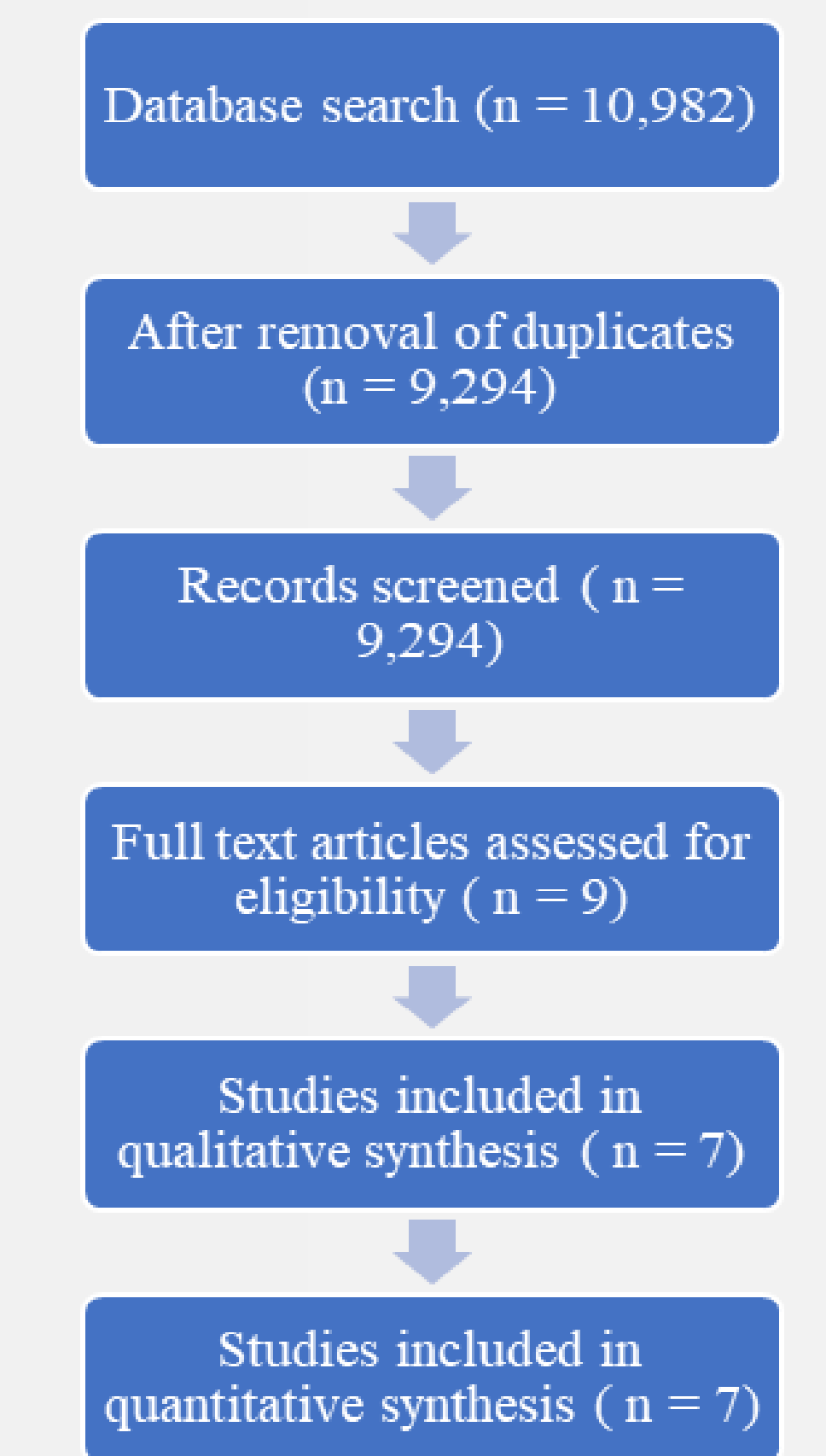


Figure 1: PRISMA flow diagram of articles screened and selected for meta-analysis



CONCLUSION

The existing literature supports that tamoxifen is not associated with an increased risk of thrombotic flap complications, total flap loss, overall flap complications, or systemic VTE.

ARTICLES SELECTED

- Billon, R., Bosc, R., Belkacemi, Y., Assaf, E., SidAhmed-Mezi, M., Hersant, B., & Meningaud, J. P. (2017). Impact of adjuvant anti-estrogen therapies (tamoxifen and aromatase inhibitors) on perioperative outcomes of breast reconstruction. *Journal of Plastic, Reconstructive & Aesthetic Surgery*, 70(11), 1495-1504. <https://doi.org/10.1016/j.bjps.2017.05.046>
- Parikh, R. P., Odom, E. B., Yu, L., Colditz, G. A., & Mykатыn, T. M. (2017). Complications and thromboembolic events associated with tamoxifen therapy in patients with breast cancer undergoing microvascular breast reconstruction: a systematic review and meta-analysis. *Breast cancer research and treatment*, 163(1), 1-10. doi:10.1007/s10549-017-4146-3.
- Kelley, B. P., Valero, V., Yi, M., & Kronowitz, S. J. (2012). Tamoxifen increases the risk of microvascular flap complications in patients undergoing microvascular breast reconstruction. *Plastic and reconstructive surgery*, 129(2), 305. <https://dx.doi.org/10.1097/2FPRS.0b013e31823ae86c>
- Samaras, S., Ashfield, S., Ali, S. F., Fopp, L. J., Benson, J. R., & Malata, C. M. (2020). Microvascular breast reconstruction and thromboembolic events in patients on hormone therapy: Audit of practice from a tertiary referral centre. *Journal of Plastic, Reconstructive & Aesthetic Surgery*. <https://doi.org/10.1016/j.bjps.2020.10.053>
- Mirzabeigi, M. N., Nelson, J. A., Fischer, J. P., Kovach, S. J., Serletti, J. M., Wu, L. C., & Kanchwala, S. (2015). Tamoxifen (selective estrogen-receptor modulators) and aromatase inhibitors as potential perioperative thrombotic risk factors in free flap breast reconstruction. *Plastic and reconstructive surgery*, 135(4), 670e-679e. doi: 10.1097/PRS.0000000000001127.
- Jokuszies, A., Radtke, C., Branski, L., Krämer, R., & Vogt, P. M. (2013). Is tamoxifen associated with an increased risk for thromboembolic complications in patients undergoing microvascular breast reconstruction?. *GMS German Medical Science*, 11. doi: 10.3205/000173.
- Salibian, A. A., Bokarius, A. V., Gu, J., Lee, Y., Wirth, G. A., Paydar, K. Z., ... & Evans, G. R. (2016). The effects of perioperative tamoxifen therapy on microvascular flap complications in transverse rectus abdominis myocutaneous/deep inferior epigastric perforator flap breast reconstruction. *Annals of plastic surgery*, 77(6), 630-634. doi: 10.1097/SAP.0000000000000707.
- Tran, B. N. N., Ruan, Q. Z., Cohen, J. B., Kamali, P., Doval, A. F., Tobias, A. M., ... & Lee, B. T. (2018). Does hormone therapy use increase perioperative complications in abdominally based microsurgical breast reconstruction?. *Plastic and reconstructive surgery*, 141(6), 805e-813e. doi: 10.1097/PRS.0000000000004359.